Beyond the threshold: Neural factors of speech perception in older adulthood

Thesis (cumulative thesis)
Presented to the Faculty of Arts and Social Sciences
of the University of Zurich
for the Degree of Doctor of Philosophy

by

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Accepted in the fall semester 2018
on the recommendation of the doctoral committee:
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Zürich, 2018

Für meine Eltern.

Abstract

A considerable part of humans' lives involves participating in spoken conversations. However, the ability to hear and understand what people say is not always guaranteed. Notably, this capacity often declines with increasing age.

For a long time, difficulties related to spoken language perception in older adulthood have been discussed in the context of declines in the auditory periphery. This thesis aims to contribute to the emerging literature examining speech perception difficulties in older adulthood as a multifactorial condition, which in addition to deteriorations in the peripheral auditory system, also encompasses cognition and central factors. Mostly focusing on central auditory factors, this thesis will begin with a general introduction, including a brief overview of frameworks of neural language processing and contemplations about neuroplasticity and speech perception in older adulthood. Based on that, it will conclude that models concerning speech processing and the brain need to be extended to older adulthood to account for the various changes related to aging regarding spoken language perception and brain function and structure. The state of research in terms of neural speech processing and aging will be discussed briefly and open questions will be identified. The introduction concludes with the aims and hypotheses of the empirical studies presented thereafter.

Within the empirical part, the first study investigated age-related differences in neurophysiological processing of prosodic speech information and its neuroanatomical correlates, extending previous research from the syllable to the word level. The second study aimed to resolve previous inconsistencies in the results of the relation between speech in noise perception and brain structure by taking into account the potential role of hearing sensitivity and cognitive abilities. Finally, in the third study, predictions from a framework of functional neuroanatomy derived from younger adults were tested in a sample of older individuals. At the same time the relation between age specific neural activation patterns and speech perception performance in the context of hypotheses of brain aging was investigated.

Finally, the results from the empirical part are discussed from different points of view. After summarizing the key findings of the three studies, implications are discussed from a theoretical, methodological, and practical perspective. Finally, remaining open questions are identified and an outlook on possible future research perspectives is given.

Zusammenfassung

Ein erheblicher Teil des menschlichen Lebens umfasst die Teilnahme an lautsprachlicher Konversation. Allerdings ist die Fähigkeit, zu hören und zu verstehen was Leute sagen, nicht immer gegeben. Insbesondere mit zunehmendem Alter nimmt diese Fertigkeit oftmals ab.

Über lange Zeit wurden die Schwierigkeiten im Zusammenhang mit lautsprachlicher Wahrnehmung zumeist ausschliesslich im Kontext von Verschlechterungen in der auditorischen Peripherie diskutiert. Die vorliegende Arbeit hat zum Ziel zum aufkommenden Feld, welches Sprachwahrnehmungsschwierigkeiten im Alter als ein multifaktoriell bedingter Zustand betrachtet und welches, zusätzlich zu Verschlechterungen im peripheren auditorischen System, auch zentrale und kognitive Faktoren umfasst, beizutragen. Diese Dissertation, die sich hauptsächlich auf zentrale auditorische Faktoren konzentriert, beginnt mit einer allgemeinen Einführung, welche einen kurzen Überblick über theoretische Modelle der neuronalen Sprachverarbeitung, sowie Betrachtungen über Neuroplastizität und Sprachwahrnehmung im Erwachsenenalter beinhaltet. Darauf aufbauend wird der Schluss gezogen, dass Modelle der Sprachverarbeitung und des Gehirns auf ältere Erwachsene ausgedehnt werden müssen, um den verschiedenen mit dem Altern einhergehenden, Veränderungen, in Bezug auf Sprachwahrnehmung und Gehirnfunktion und -struktur gerecht zu werden. Der Forschungsstand bezüglich neuronaler Sprachverarbeitung und Altern wird kurz diskutiert und offene Fragen werden identifiziert, die schließlich zu den Zielen und Hypothesen der danach vorgestellten empirischen Studien führen.

Innerhalb des empirischen Teils untersuchte die erste Studie altersbedingte Unterschiede in der neurophysiologischen Verarbeitung von prosodischer Sprachinformation und ihren neuroanatomischen Korrelaten, wobei die bisherige Forschung von der Silbe auf die Wortebene ausgedehnt wurde. Die zweite Studie zielte darauf ab, frühere Widersprüchlichkeiten in den Ergebnissen zur Beziehung zwischen Sprachwahrnehmung im Störgeräusch und der Gehirnstruktur, durch Berücksichtigung der potenziellen Rolle von Hörsensitivität und kognitiven Fähigkeiten, zu erklären. In der dritten Studie schliesslich, wurden Vorhersagen eines Modells der funktionellen Neuroanatomie, basierend auf jüngeren Erwachsenen, in einer Stichprobe von älteren Personen getestet und gleichzeitig wurde die Beziehung zwischen altersspezifischen neuronalen Aktivierungsmustern und Sprachwahrnehmungsleistung im Kontext von Hypothesen über die Alterung des Gehirns

untersucht.

Die Ergebnisse aus dem empirischen Teil werden im darauffolgenden letzten Teil unter verschiedenen Gesichtspunkten diskutiert. Nach der Zusammenfassung der wichtigsten Ergebnisse der drei Studien werden die Implikationen aus theoretischer, methodischer und praktischer Sicht diskutiert. Abschließend werden verbleibende offene Fragen identifiziert und ein Ausblick auf mögliche zukünftige Forschungsperspektiven wird gegeben.

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Acknowledgements

With this thesis marking the end of my journey as a doctoral candidate, the time has come to express my gratitude to all the people who have been part of it. First of all, I want to express my gratitude to my supervisor Prof. Dr. Martin Meyer. Thank you for putting your trust in me with this important work and guiding me through this whole process. You provided with all the resources I needed and always made sure I was able to focus on my work, which I am very grateful for. I truly appreciated that you put faith in my work even when things were not going as well as I would have wished. Last but not least, I am also grateful for your continued professional support in scientific matters. I also owe my thanks to Moritz Daum, the second member of my committee, for his involvement.

I was able to connect with and learn from a lot of researchers and fellow PhD students from different Universities around the world through the International Max Planck Research School on the LIFE Course (LIFE) program. Thus, I want to express my gratitude, to the LIFE program in general and to Prof. Dr. Alexandra Freund in particular for being given this chance.

I had the pleasure to participate in many fruitful and insightful discussions with my present and former lab colleagues, most of all Nathalie Giroud, but also Pia Neuschwander and Laura Jagoda, which I very much appreciated.

During a large part of this journey Simone Stamm and Patrick Karl Alois Neff shared a home with me. This time will forever be a fond memory to me. Thank you, Patrick, for being an almost worthy ping pong opponent and making sure that I got to eat more Indian food than ever before in my life and thank you, Simone, for being a good cooking and conversation partner, the craziest cat mom and overall the best roommate one could ever wish for.

Further thanks go to Andreas Küffer and Michel Philipp for making sure that I was working out enough, something that turned out to be desperately needed given the sharp decline in my physical fitness after your departure. I also want to thank Marcel Niklaus for the invaluable proofreading of this manuscript.

Special thanks go to Sabrina Guye, Jessica Oschwald and Dominik Güntensperger for sharing all the good and bad times with me during the last years.

Morgan Jerald, you coming into my LIFE was undoubtedly one of the best parts of this and I can never express how much you mean to me. I am thankful for your critical intellect which challenges me to think about things in different ways and to hopefully become a better person. The support and love you gave me during this time, whether it be from near or far, carried me through.

To my parents, Christine Keller and Jürg Keller, you are the foundation that I'm built on. Thank you for providing me with the environment that nurtured me, in the literal

sense of the word, but also intellectually, and ultimately led me to this point. Thank you for always trying to make sure that I could be whatever I wanted. Thank you for always being proud of what I do, even though I failed to explain it to you in a good way so often. This dissertation is dedicated to you.

Funding

This thesis was funded by the Swiss National Science Foundation (SNF, Grant no. 105314_152905 to Prof. Dr. Martin Meyer) which I am deeply grateful for. Additional financial support for hiring research assistants was provided by the Jacobs Foundation. This helped speed up the data collection considerably, which I am very thankful for. My gratitude is also owed to the University Research Priority Program (URPP) 'Dynamics of Healthy Aging' which provided the financial means to complete my research stay at the University of Michigan, Ann Arbor, USA.

Glossary

ACC anterior cingulate cortex.

ARB auditory brainstem response.

ASSR auditory steady state response.

AST asymmetric sampling in time.

BA brodmann area.

BF bayes factor.

BOLD blood oxygen level dependent.

CRUNCH compensation-related utilization of neural circuits hypothesis.

CSA cortical surface area.

CT cortical thickness.

CV cortical volume.

dB decibel.

EEG electroencephalography.

ELU ease of language understanding.

ERP event-related potential.

fMRI functional magnetic resonance imaging.

FOP frontal operculum.

FS frequency selectivity.

GMP granularity mismatch problem.

HAROLD hemispheric asymmetry reduction in older adults.

HG heschl's gyrus.

HS heschl's sulcus.

Hz hertz.

IFG inferior frontal gyrus.

kHz kilohertz.

LTM long term memory.

LTP long term potentiation.

MMN mismatch negativity.

MRI magnetic resonance imaging.

MTG middle temporal gyrus.

NHST null-hypothesis significance testing.

OIP ontological incommensurability problem.

PAC primary auditory cortex.

PASA posterior anterior shift in aging.

PFC prefrontal cortex.

POR pars orbitalis of the inferior frontal gyrus.

PTA pure tone audiometry.

PTRI pars triangularis of the inferior frontal gyrus.

SFG superior frontal gyrus.

SiN speech in noise.

SNR signal-to-noise ratio.

SPL sound pressure level.

Spt sylvian parietal temporal area.

STAC scaffolding theory of aging and cognition.

STG superior temporal gyrus.

STS superior temporal sulcus.

TC temporal compression.

TE temporal envelope.

TFS temporal fine structure.

WM working memory.

Chapter 1

Introduction

Spoken language communication is an integral part of everyday life and is a prerequisite for participation in the majority of social interactions. This human ability, however, is not static along the lifespan. In particular, difficulties with spoken language perception are likely to arise in older adulthood . As the proportion of older adults in the population is growing, the acquisition of knowledge about changes in speech perception along the lifespan becomes increasingly important. It would help to provide appropriate measures of rehabilitation and therapy in case of loss of function. Based on the axiom that the brain is essential for understanding speech, this thesis addresses the question of how neuronal processes of speech processing unfold in the older human brain and thereby aims at contribute to a better understanding of age-related changes of speech perception on a neural level. The answer to that question is assumed to be of particular importance, since it provides potential explanations for difficulties in speech perception in older adulthood that go beyond what can be explained by measures of hearing thresholds.

To set the frame for the empirical work presented in the second chapter, the introduction will begin with reviewing selected theories of functional neuroanatomy of language processing. Models of language processing in the brain will be discussed with focus on speech perception and comprehension, deliberately leaving out other language related-facilities, such as speech production or reading. It will then be advanced to make the point that this body of research is insofar incomplete as its assumptions and hypotheses are derived from research on predominantly younger samples. The argument will be made that these models are not directly applicable to older adults. Research suggests that the brain undergoes plastic changes during the entire lifespan, with some of these changes being specific to older adulthood. At the same time, the occurrence of changes in hearing and speech comprehension, such as hearing-loss, is increasingly likely with advancing age. Thus it seems plausible to assume that speech processing is different in older adulthood.

Based on these premises, it will then be moved on to first discuss previous findings about how structure and function of the brain change along the lifespan in general,

followed by a discussion of central hypotheses. In the last part of this chapter, the state of research related to neural speech processing in older adulthood will be discussed, and some of the open questions will be highlighted. To conclude the introduction, the research questions, that guided this thesis, will be derived from the open issues identified previously.

1.1 Brain and language

In the first part of this chapter, the origins of frameworks of the functional neuroanatomy of speech processing will be reviewed and issues inherent to those models will be identified. Advances in brain imaging techniques that eventually led to extensions and refinements of the classical models will be discussed shortly, with a focus on procedures relevant for the empirical part. Contemporary frameworks of neural speech processing that include findings drawn from these methodological advancements will be reviewed thereafter.

Despite the knowledge accumulation in the domain of brain and language research enabled by these models, they suffer from several limitations. In particular, they mainly rest on mapping language functions onto brain regions without providing a mechanistic description of how the computations related to language are carried out by the brain. The question of whether these models can provide an adequate approach in describing the relationship between linguistic concepts and the neural processing of language will thus be addressed. The end of this section will introduce a model that aims to fill this gap and thus may be better able to describe relationships between brain and language.

1.1.1 Moving past the classical model

The classical models

Major milestones for research on the brain and language were reached with the seminal works of Paul Broca (Broca, 1861, 1865) and Carl Wernicke (Wernicke, 1874) in the 19th century. In their work, they described language disorders observed in patients with cortical lesions. Using post-mortem examinations of those patients' brains, they were able to map the language deficits previously observed in the living patients to cortical lesions from the autopsy. This led Wernicke to formulate a model of how language is represented in the brain, which was later refined by Ludwig Lichtheim (Lichtheim, 1885) and Norman Geschwind (Geschwind, 1970, 1974) and is referred to as the Wernicke-Lichtheim-Geschwind model [1].

[1] The term "Wernicke-Lichtheim-Geschwind model" is sometimes used to refer to a very specific model. In this thesis however, the term will be used to refer to the entire family of models that build on the assumption that there are two main language centers connected by the arcuate fasciculus.

In its essence, the model states that an anterior frontal area is critical for speech articulation, while a posterior superior temporal area is responsible for speech perception. Further, it was argued that these two areas are connected through a fibre tract called the arcuate fasciculus enabling communication between those regions. Accordingly, in the past, these regions have often been referred to as the "articulate-" and the "perceptual speech center". These models proved to be fruitful because they provided presumed etiologies for various types of aphasias. Roughly speaking, speech production deficits were attributed to lesions in the anterior frontal region, speech perception deficits to injuries in the superior temporal region, and deficits in speech repetition to damages to the arcuate fasciculus.

However, in recent decades, major advances in in-vivo brain imaging techniques have led to findings that raised severe doubts about the appropriateness of the classical model. Most of all, the invention of magnetic resonance imaging (MRI) and the renaissance of EEG (EEG) spurred a substantial amount of research, in neuroscience in general, and also in the study of the relationship between language and the brain.

Neuroimaging methods

MRI is a technique that utilizes strong magnetic fields to visualize different types of tissues inside an organism. This is made possible by the fact that different types of tissue have different magnetic properties that can be measured with MRI. By using MRI, it is possible to create three-dimensional images of the anatomy and function of the brain. Depending on the imaging parameters used, different types of tissues can be made depicted. So called 'T1-weighted' imaging sequences allow for distinguishing between cerebrospinal fluid (CSF) and white and gray matter and are preferentially used for the analysis of brain structure.

Another popularly used sequence is called 'T2-weighted' and permits the measurement of brain function. This is usually done within an experimental setup, where brain responses are measured in response to a stimulus. Similar to different types of tissue, blood has distinct magnetic properties depending on its oxygen saturation. The oxygen saturation of the blood in the brain is assumed to be a proxy of neural activity because active neurons have an increased need for energy, which is reflected by an increased oxygen saturation of the blood in the vicinity of the cell. Thus, areas with increased levels of oxygenated blood are considered to be involved in neural computations ocuuring during the time of measurement. This is called the blood oxygen level dependent (BOLD) effect, and the related technique is called functional magnetic resonance imaging (fMRI). (For the sake of completeness, it should be mentioned that fMRI can also be applied to design setups where no stimulus is delivered to the participant to measure brain function at "rest" (resting-state fMRI).)

A main advantage of fMRI, as compared to lesion-based approaches, is that it in-

creases the anatomical precision, while at the same time potentially avodding confounding effects of brain lesions, namely brain reorganization processes that take place after an injury (Price, 2012). This means, that researchers are able to acquire images with high spatial resolution at any given time (not only after the passing of the person to be investigated). In addition to high spatial resolution, its ability to measure individuals in-vivo and its ability to estimate brain function, MRI is non-invasive, does not expose the subject to radiation, and does not require contrast agents to produce an image (Glover, 2011). Hence, the popularity of MRI rests on its ease of use, its high level of safety and its many possible applications.

However, a major drawback of fMRI is that the temporal resolution is low. This is mainly because of the shape of the hemodynamic response, which has a width of around 3 seconds and arises around 5-6 seconds after the occurrence of the stimulus (Glover, 2011). Thus, since neural events take place on a subsecond scale, fMRI is not able to capture these events with great temporal fidelity.

Other approaches, with higher temporal resolution, such as electroencephalography (EEG[2]), are better suited to capture the temporal dynamics of brain function. EEG makes use of the fact that synchronous electrical activity of nerve cell populations in the brain cause voltage fluctuations, which are measurable on the surface of the head. Thereby, these voltage fluctuations caused by the discharging of neurons are derived from electrodes on the surface of the head. EEG thus provides a direct measure of neuronal firing. As mentioned above, the sampling rate of EEG is much higher compared to fMRI, i.e. several hundred sampling points per second. Thus, neural events can be captured on a much more fine grained temporal scale than what is possible by using fMRI. The EEG signal can be analyzed in the time domain (e.g. event-related potentials (ERP)), the frequency domain (e.g. EEG power spectra) and also the time-frequency domain (e.g. wavelet analysis), where each of these can inform different questions regarding brain functioning. Similar to (f)MRI, EEG is a non-invasive and safe technique that does not require much preparation for the participant, with the advantage of high temporal resolution, and is thus comparably popular within neuroscience research.

The spatial resolution available from EEG, that is identifying the location of the neural sources producing the activation, is, however, limited. The only spatial information provided by the EEG is the position of the electrodes on the scalp. Thus, there is no direct information available about the whereabouts of the neural sources of scalp voltage fluctuations within the brain[3]. Apart from (f)MRI and EEG, a range of other methods exist too, however, since the main focus of the work at hand is on EEG and (f)MRI, this

[2]EEG is technically not a neuroimaging technique because, in contrast to (f)MRI, it does not produce images of the brain. For the sake of simplicity and brevity, when referring to neuroimaging methods, neurophysiological methods are included too.

[3]It should be mentioned here that approaches exist to estimate the sources of the electrical signal measured on the scalp (e.g. Pascual-Marqui, Michel, & Lehmann, 1994).

chapter will not discuss them.

In summary, MRI and EEG can provide complementary information in terms of spatial and temporal resolution and suitability of each method depends on the question aimed to be answered.

A critique of the classical models

So what have scientists learned about language and the brain having these methods at their disposal? Regarding the Wernicke-Lichtheim-Geschwind model, the main conclusion drawn by researchers is that, despite having had a stimulating impact on neuroscientific language research and as a clinical guideline, the classical model is outdated, when findings from neuroimaging are taken into account. For example, Poeppel and Hickok (2004) argue that the model suffers from various drawbacks, namely, that it cannot account for the symptom complex of aphasia, that it incorporates an overly simplistic linguistic model, and that it suffers from anatomical problems. They argue that Broca's aphasics also show comprehension deficits, which, according to the classical model, would not be expected since Broca's area is not assumed to be involved in the perception of language. Further, they reason that dividing language in an articulate and a perceptive facility is too coarse of a division, since it neglects linguistic concepts such as syntax and semantics (they also state, however, that these concepts might still be too coarse (see also Chapter 1.1.2)). Finally they point out that the number of regions involved in language processing by far exceeds the number of regions included in the classical model. For instance, results from a meta-analysis show that numerous regions distributed over peri-sylvian, frontal and parietal areas are involved in language processing (Vigneau et al., 2011).

Along the same line, P. Tremblay and Dick (2016) argue in favour of abolishing the terms Broca's and Wernicke's (i.e. the terms that have been popularly used to refer to the regions within the classical model) area. In addition to the points already made by Poeppel and Hickok (2004), they stress that the model is also under-specified in terms of white matter connectivity and that there is no agreed upon definition about the location of Broca's and Wernicke's area. Anatomical definitions of Wernicke's area range from encompassing posterior parts of the superior temporal gyrus to the inclusion of large temporo-parietal areas. The same is true for Broca's area: depending on the author different parts of the inferior frontal gyrus are assumed to constitute Brocas area (for a depiction of the different anatomical definitions of Broca's and Wernicke's area, dependent on the author, see P. Tremblay and Dick (2016)).

Other examples of anatomical issues pertain to the macro- and cytoarchitecture of these regions. For example, the frontal operculum, an area usually overlapping with anatomical definitions of Broca's area, consists of macro- and cytoarchitecturally distinct subregions, possibly related to different functional roles (Friederici, 2011).

Due to these shortcomings, several efforts have been made in past years to extend, correct and improve the Wernicke-Lichtheim-Geschwind models. Some of the most influential models, focusing on aspects of speech perception, will be reviewed in the next section.

1.1.2 Contemporary models of the functional neuroanatomy of language

Hemispheric language dominance

One of the most prominent implications of the classical Wernicke-Lichtheim-Geschwind models is that the left hemisphere is the language dominant hemisphere. This particular notion had already been challenged before the age of neuroimaging began. For instance, Ross (1981) noted that sometimes, patients with right-hemispheric lesions also suffered from language disorders. Notably, patients exhibited difficulties with the processing of emotional features of language. Some years later, the task-dependent hypothesis was put forward, stating that the right hemisphere might be dominant for the processing of emotional aspects of language, while the left hemisphere is responsible for its propositional aspects (Van Lancker, 1980).

This notion, however, turned out not to be sustainable, since it had been demonstrated thereafter that damage to the right as well as to the left hemisphere can affect the processing of propositional as well as emotional aspects of language (Behrens, 1989; Pell & Baum, 1997; Ross, Shayya, & Rousseau, 2013; Weintraub, Mesulam, & Kramer, 1981; Witteman, van IJzendoorn, van de Velde, van Heuven, & Schiller, 2011). Nonetheless, it became evident that not only was the left hemisphere involved in language processing but also, at least to some extent, the right hemisphere. This notion was corroborated by meta-analyses demonstrating left and right hemispheric contributions to language processing (Vigneau et al., 2011).

With time, evidence from neuroimaging led to a particularization of hypotheses about the localization of language functions in the brain. A model, based on evidence acquired over the first years of fMRI, states that auditory processing of heard words activates bilateral superior temporal gyri, while word meaning is accessed in left posterior middle temporal, posterior temporoparietal and anterior inferior temporal cortices (Price, 2000). Thus, the model acknowledges bihemispheric involvement in speech perception and provides more clear-cut anatomical descriptions of regions assumed to be involved in spoken language processing that extend the number of regions included in the classical model.

Mapping function to structure

In the following, several attempts have been made to map linguistic functions to brain structure. In reference to the two-stream hypothesis (Milner & Goodale, 2006), which states that there are two conceptually distinct processing pathways in the visual system (i.e. a pathway that is responsible for the spatial location ("where") and a pathway that is involved in the identification ("what") of visual objects), Hickok and Poeppel (2004) subsequently proposed the dual-stream model of language processing. They advance the idea that after initial analysis of auditory input in bilateral superior temporal regions, auditory representations are further processed in two conceptually different processing pathways.

In an analogy to the visual system, and according to their anatomical location, the two streams have been called the "ventral" and "dorsal" streams. While the ventral stream is thought to be involved in sound-to-meaning-mapping, the dorsal stream was suggested to be involved in sound to articulatory-based representation mapping. According to the dual-stream model of language processing, initial spectrotemporal analysis takes place in bilateral dorsal superior temporal gyrus (STG). Subsequently, auditory input is submitted to a phonological network, which is located in the middle and posterior superior temporal sulcus (STS), where phonological analysis takes place. After this stage of processing, the stream is branched into two parts.

The ventral stream proceeds to posterior middle and inferior portions of the temporal lobe where lexical processing, relying on the phonological information acquired in the preceding step, is thought to take place. This part of the ventral stream is hypothesized to be mainly bilaterally organized, whereas the subsequent computations, which involve combinatorial processes such as syntax processing, are located in anterior portions of the left hemispheric temporal lobe.

The dorsal stream involves an area referred to as sylvian parietal temporal (Spt), which is located at the parietotemporal boundary in the Sylvian fissure, posterior inferior frontal gyrus (IFG) and premotor cortex. This pathway executes computations related to sound to meaning mapping and includes a sensorimotor interface (area Spt) and an articulatory network (posterior IFG and premotor cortex). In contrast to the ventral stream, this network is assumed to be left-lateralized.

Since two fibre tracts can be found within each pathway (i.e. fasciculus arcuatus and fasciculus longitudinalis superior in the dorsal path and capsula extrema and fasciculus uncinatus in the ventral path), it has been stated that the ventral and dorsal stream, in fact, consist of two pathways each (Friederici, 2011, 2012). Thereby, one of the two dorsal pathways is assumed to support sound-to-motor mapping, while the other dorsal pathway is thought to be involved in higher level language processing, such as syntactic processing. Yet, little is known about potentially different functions of the two ventral

paths (Friederici, 2012).

According to Friederici (2012), after initial auditory analysis takes place in the primary auditory cortex (PAC), which is located in bilateral Heschl's gyrus (HG), initial syntactic and lexical-semantic processes are carried out in several portions of the temporal cortex. The IFG is assumed to be involved in higher-order language computations, where the frontal operculum (FOP) and pars opercularis seem to carry out syntactic processes, while the pars triangularis and orbitalis are thought to be involved in semantic processes. As stated by Friederici (2012), a region in the posterior temporal cortex is responsible for semantic and syntactic integration. In contrast to syntactic and semantic language processing, the processing of prosody is assumed to take place in the right hemisphere (Friederici & Alter, 2004; Poeppel, 2003; Zatorre, Belin, & Penhune, 2002).

Issues related to contemporary models

While in most cases authors agree that the language network consists of the PAC and regions located in the temporal and frontal lobes and that it is at least in part bilaterally organized, there is a debate about which specific regions are part of the language network and what specific functions are assigned to each region.

For example, Hagoort (2005, 2013), in contrast to Friederici (2012), suggest that integration – or unification in his terminology – is performed exclusively in the IFG (including Brodmann areas (BA) 44, 45, 47 and 6). In his model, he assumes that language processing rests on three core processes, namely memory, unification and control. According to him, language arises from the retrieval of lexical items from memory and the combination of them into larger structures. This unification process is taking place in different representational levels, that is syntactic, semantic and phonological. Finally, control refers to the executive functions needed to comprehend and produce language, such as attention.

While, as stated before, the model assumes unification processes to take place in inferior frontal regions, memory processes are assigned to areas in the temporal cortex and control regions are located in the frontal lobe dorsal to the unification region, as well as to the anterior cingulate cortex (ACC) and attention related areas. Along the same lines, no consensus exists, for instance, in terms of which specific brain regions are implicated in the dorsal and the ventral stream (Fridriksson et al., 2016).

Another issue pertains to the question of whether a function is distinctively localized within a cortical region or whether it is carried out by distributed neural ensembles (Blank, Balewski, Mahowald, & Fedorenko, 2016). For example, in the case of syntax, some researchers support a more locally restricted view, assigning syntax processing to temporal and frontal regions (e.g. Friederici, 2011, 2012; Hagoort, 2005, 2013), while others argue for a more distributed neural processing of syntax (Blank et al., 2016).

These examples illustrate that the mapping of linguistic functions to brain regions

or the definition of a functional neuroanatomy is, at this time, still a matter of debate within several domains.

However, besides the debates about the cortical organization of language and the resulting lack of a unifying, comprehensive neurobiological model of language processing, another criticism concerns the relationship between neuroscience and linguistics (Poeppel, 2012; Poeppel & Embick, 2005). Two main problems have been identified, dubbed the *maps problem* and the *mapping problem*.

Within the *maps problem*, researchers question whether mapping linguistic functions to brain areas can give explanatory insights into the mechanics of the neural underpinnings of cognitive functions. Put differently, mapping cognitive functions to cortical locations can tell *where* in the brain certain tasks are carried out but nothing is known about *how* the brain processes information. At the same time the *mapping problem* emphasizes that models of functional neuroanatomy have previously failed to establish formal relationships between linguistic and cognitive theories and brain function.

According to Poeppel and Embick (2005), this is due to two shortcomings. The first shortcoming, which is called the granularity mismatch problem (GMP), states that fundamental operations of linguistics and neuroscience are of different granularity (e.g. linguistics: concatenation, neuroscience: long-term potentation (LTP)), meaning that there is no correspondence of operations between the two domains. The second shortcoming, which is called the ontological incommensurability problem (OIP), states that the fundamental elements of linguistics and neuroscience have not been matched up with each other thus far (e.g. linguistics: syllable, neuroscience: neuron).

In other words, there is no direct link between neuroscience and linguistics, neither for the fundamental operations nor for the fundamental elements.

Overcoming the present issues

One attempt to tackle this problem is provided by the asymmetric sampling in time (AST) hypothesis (Doelling, Arnal, Ghitza, & Poeppel, 2014; Giraud & Poeppel, 2012; Poeppel, 2001, 2003). The AST hypothesis aims to describe the spectrotemporal analysis of speech signals by the brain. A speech signal can be characterized as sound pressure waves unfolding over time, consisting of various frequencies, amplitude and phases. Thereby rapid fluctuations, that is temporal fine structure (TFS), characterize speech features on a segmental level, such as phonemic information, and slower fluctuations, that is temporal envelope (TE), represent suprasegmental features, such as prosodic information (Meyer, 2008).

The AST hypothesis states that TFS and TE are sampled by the brain by neural oscillations, i.e. the synchronized firing of neuronal populations, of similar frequencies. In particular, TFS information is sampled by lower γ-band oscillations ($\sim$ 40 Hertz (Hz)) and TE information by θ-band oscillations ($\sim$ 4 Hz). In other words, speech information

is integrated by the brain on different time scales. TE information is sampled by longer ($\sim$ 250 ms) and TFS by shorter time windows ($\sim$ 25 ms).

According to the hypothesis, the brain is able to sample the speech information by entraining its oscillations to the speech signals. Entrainment describes a situation where neural oscillations synchronize their phase to the phase of the speech signal (or, in general, to incoming stimulus information), enabling the representation of these features of the auditory input. Different potential functions of this mechanism have been put forward that either emphasize the role of entrainment to the TE as an analytic or synthetic tool (Ding & Simon, 2014).

Proponents of the former view hypothesize that cortical entrainment extracts primitive auditory features within the auditory input (Ding & Simon, 2011; Howard & Poeppel, 2012) while proponents of the latter propose cortical entrainment be responsible for the integration of features into linguistic units (Ding & Simon, 2012; Golumbic et al., 2013; Schroeder, Lakatos, Kajikawa, Partan, & Puce, 2008). Hence, neural entrainment is a mechanism that is critical for the decoding and integration of features of speech prosody (Meyer, Keller, & Giroud, 2018).

The AST model thus offers a perspective directly linking linguistic concepts (i.e. spectrotemporal speech information) with neurobiological concepts (i.e. neural oscillations) and hence offers a potential way to overcom the problems outlined above.

A further prediction of the AST model pertains to the anatomical localization. This type of spectrotemporal analysis is thought to be carried out in posterior regions of the STG bilaterally involving regions outside the PAC. An additional assumption of the model is that this kind of spectrotemporal processing is asymmetric in terms of hemispheric lateralization. More specifically, right hemispheric auditory areas are assumed to preferentially process TE, information while left hemispheric areas primarily process TFS information (see Figure 1.1).

The AST hypothesis has been supported by a number of studies in recent years (Boemio, Fromm, Braun, & Poeppel, 2005; Geiser, Zaehle, Jancke, & Meyer, 2008; Hesling, Clément, Bordessoules, & Allard, 2005; Hesling, Dilharreguy, Clément, Bordessoules, & Allard, 2005; Hurschler, Liem, Jäncke, & Meyer, 2013; Hurschler, Liem, Oechslin, Stämpfli, & Meyer, 2015; Liem, Hurschler, Jäncke, & Meyer, 2014; Meyer, Alter, Friederici, Lohmann, & von Cramon, 2002; Plante, Creusere, & Sabin, 2002; Zaehle, Wüstenberg, Meyer, & Jäncke, 2004; L. Zhang, Shu, Zhou, Wang, & Li, 2010) and seems to be rooted in intrinsic oscillatory properties of auditory areas in the respective hemisphere (Giraud et al., 2007; Morillon, Liégeois-Chauvel, Arnal, Bénar, & Giraud, 2012) possibly related to anatomical peculiarities of left and right auditory cortices (i.e. pyramidal cell size, myelination and cortical column spacing: Gray & McCormick, 1996; Hutsler & Galuske, 2003; Penhune, Zatorre, MacDonald, & Evans, 1996; Seldon, 1981; Traub, Buhl, Gloveli, & Whittington, 2003).

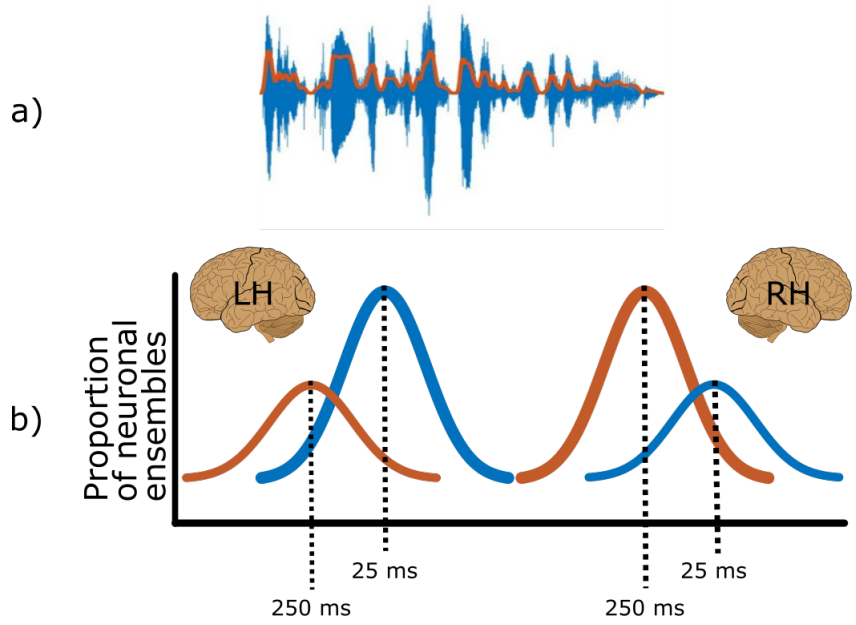

Figure 1.1. Depiction of the AST model. a) Soundwave with visualization of TE (orange) and TFS (blue) information. b) Hemispheric preferences for different temporal integration windows related to TE and TFS (redrawn after Giraud et al. (2007)).

It has also been suggested that the AST model could help to overcome an issue related to linguistics, namely how the term "prosody" is defined (Ladd, 2014). In particular, Ladd (2014) hypothesizes that the mechanisms proposed by the AST framework might provide empirical grounds for defining "prosody" as set of phenomena that can be distinguished from segmental phonology (see Meyer et al. (2018) for a more extensive discussion of the relationship between prosody and the brain). In that sense, the study of the brain could help to explain something about language, thus speaking to one point of the critique raised by Poeppel and Embick (2005), regarding the lack of insights about language from neuroscientific research.

Intermediate summary

Language research from the first decades of neuroimaging has brought various new insights about which cortical areas are involved in the language network and have led to the abandonment of the classical model of language processing in the brain. Most notably, it is acknowledged that both left hemispheric and right hemispheric areas are involved in the language network and, implicit in the assumption of a network organization of language, the notion that speech is organized in "language centers" has been abolished. There is consensus among most scholars that major language relevant regions are located in IFG and temporal lobe, namely in the superior (STG) and middle temporal gyrus (MTG, Friederici (2011)).

However, some issues remain. One issue that is common to these approaches is

that they focus on localizing linguistic concepts in the brain but do not provide any propositions about how the operations related to these linguistic elements are represented in the brain. The AST model aims to overcome this issue by proposing a direct link between linguistics and brain function and structure and can thus be considered an ideal working hypothesis. Still, this model, as well as all the others, is mainly based on data from younger adults. In the next, section arguments will be provided regarding why the extension of neurobiological models of speech perception to different age groups is important and needed.

1.2 Towards a lifespan approach

The vast majority of the research in psychological science is based on investigations of subjects from western, educated, industrialized, rich and democratic societies, namely college students, and it has been argued that the samples drawn from these populations are unlikely to be representative of humankind more broadly (Henrich, Heine, & Norenzayan, 2010). While this argument is mainly made with respect to the cultural background of research participants, there are good reasons to argue it also holds true in relation to human aging. A comprehensive model of neuronal speech processing, therefore, should not only be generalizeable across cultures but also take into account a person's life stage. The present section reviews arguments against a generalization of models of neural speech perception from younger to older populations.

In the first part, it will be argued that the human brain is plastic throughout the lifespan which implies that neural processing is different in different stages of the lifespan. Examples of neural plasticity in general and of language processing specifically will be discussed.

The second part reviews differences between age groups in hearing and speech comprehension. The argument will be made that these differences either have consequences for how the brain processes speech or are a consequence of changes in brain function and structure themselves. Next, the conclusion will be made that it is unlikely that models of brain and language based on younger samples are well suited to describe neural speech processing in the aging brain.

Finally, it will be called for an extension of models of neural speech processing to account for differences that are particular to older adulthood.

1.2.1 The plastic brain

Lifelong neuroplasticity

The terms neural and brain plasticity are closely related to the rejection of a long-standing doctrine in Psychology, stating that, after neural maturation is reached in young

adulthood, the brain's structures remain largely unchanged. Accumulated evidence in past years, however, has made it increasingly clear that changes of the brain can occur throughout the lifespan (Lillard & Erisir, 2011).

Neural plasticity can broadly be defined as the reorganization of the nervous system in response to changes in the environment or within the organism (Pascual-Leone, Amedi, Fregni, & Merabet, 2005). Neuroplastic changes can arise on several levels, including neurogenesis, synaptogenesis, changes in nerve cell morphology, axon and dendrite growth or movement, myelination, increases in glial cell size and number, angiogenesis, and changes to neural circuits and cortical fields (Lillard & Erisir, 2011; Zatorre, Fields, & Johansen-Berg, 2012). These neuroplastic changes unfold on different time scales and the likelihood of their appearance varies along the lifespan. For example, neurogenesis takes place within days and is seen frequently in the juvenile period but is limited in adulthood to the hippocampus and the olfactory bulb. Others, such as the growth of new axon boutons and dendritic spines, occur within minutes and are assumed to take place in younger and older individuals.

Neural plasticity is separate from neural development in that the latter describes neural reorganization processes that are programmed within the genetic code, while the former describes neural changes occurring due to external stimulation or internal changes (Lillard & Erisir, 2011). The terms critical and sensitive periods fall into the realm of neural development and refer to developmental periods of increased sensitivity for the acquisition of a certain skill or ability due to a favourable state of the nervous system at this period in time. The assumption is that after the passing of these periods, related skills can not be acquired anymore (critical period) or can only be achieved within specific circumstances (sensitive period), such as increased input (Lillard & Erisir, 2011).

Thus, neural plasticity refers to neural reorganization that is different from neural development and that occurs throughout the entire life span, albeit at different levels and to different degrees.

Examples of neuroplasticity

Neuroplastic events can be driven by different triggers. Reorganization processes can, for example, be seen in reaction to *sensory deprivation*. An example of such reorganization processes in relation to sensory deprivation is visual cortex activation during verbal tasks in congenitally blind individuals (Amedi, Raz, Pianka, Malach, & Zohary, 2003). In this study, visual areas in the occipital cortex were active during verbal tasks in blind individuals, while no such activation could be found in sighted participants. Hence, regions that are involved in visual processing by default, but are devoid of visual input, were active during verbal processing. This represents a case of so called *cross-modal plasticity*, where areas that are deprived from their original input become involved in the processing of other domains, that is areas deprived of sensory input are taken over by

another domain.

Another factor that triggers neural plasticity is *experience*. A famous example of experience dependent plasticity is the relation between the volume of the hippocampus, a structure thought to be involved in the consolidation of memories, and spatial navigation experience (Maguire et al., 2000). They found that the volume of a sub-region of the hippocampus was significantly larger in taxi drivers than in controls and that the volume was positively correlated with the time spent driving a taxi. It was speculated, that hippocampus volume increases with increasing proficiency in spatial navigation, such as is the case when driving a taxis for a longer time because of the memorization of the street map of a city. This type of plasticity is usually termed *experience-dependent plasticity*, that is, changes in the brain occurring due to changes in behaviour.

However, due to the correlational nature of the study, these effects can not be causally interpreted. Thus, it is unclear whether taxi driving led to changes in brain structure or whether individuals with larger hippocampi were more likely to spend more time working as taxi drivers because they had better spatial memory to begin with.

Work reporting neuroplastic changes after mastering basic juggling skills addressed this issue about causality of effects (Draganski et al., 2004). In this experimental study, MRI was recorded before participants started a juggling training, shortly after they had acquired basic juggling skills and after a 3 months follow up period. Learning to juggle led to a significant increase in gray matter in visual areas related to perception and spatial anticipation of moving objects, which was not seen in a control group of non-jugglers. This indicates that the change in behaviour caused brain structure changes. Training spurred plastic processes that led to beneficial changes in the brain.

Since these processes allow an individual to adapt to environmental changes in a beneficial way, they are referred to as *adaptive* plastic changes. However, plastic processes can also lead to adverse effects for the individual, in which case these phenomena are generally referred to as *maladaptive* plasticity. Usually maladaptive plasticity is observed after neuronal maladjustment to alterations in sensomotoric input. Maladaptive plasticity as a direct consequences of loss of sensory input have, for instance, been proposed for the generation of tinnitus (Shore, Roberts, & Langguth, 2016) or phantom limb (Flor, Nikolajsen, & Jensen, 2006). In these cases, areas originally processing input from deafferentiated regions – due to hearing loss in the case of tinnitus or amputation in the case of phantom limbs – exhibit abnormal firing patterns after the loss of input that lead to the phantom percept (i.e. phantom sound in tinnitus and phantom sensation or pain in phantom limb).

Maladaptive plasticity can also make readjustment to restored function more difficult. Examples include the application of cochlear implants after deafening (Sandmann et al., 2012) or motor recovery after stroke (Takeuchi & Izumi, 2012). In particular, cross-modal plasticity in auditory regions can impede the beneficial effect of cochlear implants

and altered neural activation caused by compensatory movements after a stroke can hinder the return to normal motor patterns.

In conclusion, neural plasticity is a lifelong process, triggered by different events, on a functional or structural level, with either having benign or a malign outcomes for the affected individual.

Plasticity of the auditory system

After having established that the human brain is able to change continuously along the lifespan, whether it be due to changes in behaviour and environment or due to changes within the individual, the question of whether plastic events can be observed within the domain of language will be addressed next. Although language is often seen as a prime example to illustrate the concept of sensitive or even critical periods (Kuhl, 2004, 2010), neuroplastic changes in the auditory system still occur after these periods have passed (White, Hutka, Williams, & Moreno, 2013; Y. Zhang & Wang, 2007).

One example of plasticity of the auditory system is recovery in aphasia after a stroke. It has been reported that patients with post-stroke aphasia showed activation shifts towards the right hemisphere in regions affected by the stroke with time of recovery (e.g. Thulborn, Carpenter, & Just, 1999). An early hypothesis related to post-stroke aphasia plasticity is that the right hemisphere compensates for damage done to the left hemisphere caused by the stroke (Karbe et al., 1998).

However, it has also been reported that areas ipsilateral to the lesions can be recruited for compensation as well and that the involvement of the right hemisphere is probably dependent on various factors, such as time after stroke (Hartwigsen & Saur, 2017; Heiss & Thiel, 2006; Schlaug, 2018). This research shows that in case of insult to areas relevant to language processing, the brain is able to reorganize in order to counteract loss of function related to the lesions. Thus, similar to other modalities, the auditory system seems to be able to reorganize after internal changes in order to ensure maintenance or recovery of function.

In addition language areas are not only susceptible to plastic processes after damage to the brain, but also language experience itself shapes the brain. In tonal languages, such as Mandarin or Thai, different word meanings can be signaled trough different pitch contours. In contrast to speakers of non-tonal languages, such as English, where pitch processing mainly takes place in right hemispheric areas (see Chapter 1.1.2), lexical tone processing is located predominantly in left hemispheric brain circuits in speakers of tonal languages (Gandour et al., 2003, 2004, 2002a, 2002b). Thus, the lateralization of acoustic cues is different depending on the linguistic relevance of these cues in the listeners native language.

However, research investigating learning in adulthood has demonstrated that learning of a second language leads to structural plastic changes in the brain (Mechelli et al.,

2004). In this study, gray matter density of English and Italian bilinguals was measured. Results showed that in comparison to monolinguals, bilinguals showed more density of gray matter in a left inferior parietal area, which the authors related to verbal-fluency tasks. The same areas were positively correlated with proficiency in and negatively correlated with age at acquisition of the second language.

Hence, grey matter in left hemispheric parietal areas was denser the earlier individuals learned a new language and the more proficient they were in that language. This line of research suggest that language networks are shaped according to the linguistic environment a person finds themself in. However, these findings do not speak themselves for the occurrence of plastic events after sensitive periods but are presumably a consequence of increased sensitivity to phonological peculiarities within ones native language and a decreased sensitivity thereof for foreign-languages (Kuhl, 2004).

Thus, the question of whether experience-dependent plastic reorganization in adult human auditory system can take place might be informed by research on language learning in adulthood. Structural plasticity in response to language learning has been demonstrated by Stein and colleagues (2012). In this study English native speakers who were learning German were measured twice at the beginning and at the end of a five month period. Results demonstrated that increases in gray matter density in the left inferior frontal gyrus were correlated with increase of German skills. Interestingly, it was not absolute gray matter that was predictive of learning but the relative increase within the time period. This was taken as evidence that brain structure changes reflect individual amount of learning independent of the absolute proficiency.

This finding is mirrored on the functional level by earlier research from the same group (Stein et al., 2006). In a similar longitudinal setting, differences in the ERP responses to German words were observed in a group of native English speakers before and after learning German. In particular, ERP latency differences were observed, indicating a faster processing of German words after the learning period.

Another instance for neural plasticity in response to language learning was reported by Callan et al. (2003). Native Japanese speakers trained perceptual identification of /r-l/ phonetic contrast, which is not relevant in Japanese and thus difficult to distinguish for native speakers. Differences in neural activation were evident after a one month training period. Neural reorganization, in terms of increased hemodynamic responses, could be observed in various regions related to acoustic-phonetic processing, as well as in areas related to verbal speech processing and learning.

Thus, experience-dependent neuroplasticity on the functional as well as the structural level are evident in the auditory system in the context of language learning (P. Li, Legault, & Litcofsky, 2014).

Intermediate summary

The brain can be seen as a plastic organ, which adapts to changes in inputs (e.g. sensory decline, experience) but also to changes within itself (e.g. brain injuries). Plasticity is seen as a lifelong process that is not limited to critical or sensitive developmental periods. Included in these plastic processes is the neural reorganization of language circuits, be it due to insults to the brain or changes in auditory input, such as language learning, on the structural and the functional level.

Thus, it is concluded that the brain is a dynamic entity, which implies that models of neural processing, such as models of neural speech perception, need to take into account that there is no one-size-fits-all solution when aiming to describe speech perception for the entirety of all humans. In the next part, external and internal changes influencing structure and function of the auditory system specific to older populations will be reviewed.

1.2.2 Hearing and speech understanding in older adulthood

Peripheral hearing loss

One of the most striking findings in relation to speech perception and aging is that with increasing age hearing sensitivity decreases (Brant & Fozard, 1990; Cruickshanks et al., 1998; Roth, Hanebuth, & Probst, 2011; Wiley, Chappell, Carmichael, Nondahl, & Cruickshanks, 2008). This phenomenon is often termed age-related hearing loss or presbycusis [4] and is the third most chronic condition in adults older than 65 years (Yueh, Shapiro, MacLean, & Shekelle, 2003). The gold standard to measures hearing sensitivity is pure tone audiometry (PTA). In this procedure, the person under investigation listens to sine tones of different frequencies. For each of these tones the sound pressure level (SPL) in decibel (dB) is assessed for which the tone in question is still audible to the participant. Usually, presbycusis starts in higher frequencies and progresses to the frequency range between 2 and 4 kilohertz (KHz) which is important for the comprehension of voiceless consonants (Gates & Mills, 2005).

Different types of pathologies are involved in the expression of presbycusis including sensory, neural, metabolic and mechanical hearing loss (Schuknecht, 1964). The most common among these pathologies is sensorineural hearing loss, which includes pathologies in the organ of corti (sensory) and the auditory nerve (neural) (A. C. Wong & Ryan, 2015).

Sensory hearing loss affects the inner ear where the cochlea, which holds the organ of corti, is located. The organ of corti hosts hair cells that transform the vibrations caused by sound pressure waves that have been transmitted from the outer ear over the

[4] The terms age-related hearing loss and presbycusis will be used synonymously for the remainder of this thesis.

tympanic membrane and the ossicles to the cochlea, into an electrical signal. Sensory hearing loss refers to the deterioration of these hair cells and the inability to transform the acoustical signal into an electrical signal and is most closely related to high-frequency hearing loss.

Neural hearing loss, in the sense of Schuknecht (1964) refers to loss or degeneration of neurons in the auditory nerve. The other pathologies, are, according to Schuknecht (1964), loss of metabolic functioning due to deterioration of the stria vascularis (metabolic) and stiffening of the basilar membrane (mechanic).

Age-related hearing loss was in practice conceived as elevated thresholds in PTA (Humes et al., 2012), however reduced speech understanding in noisy environments, slowed central processing of acoustic information and impaired localization of sound source are characteristic for presbycusis as well (Gates & Mills, 2005).

Among the symptoms of age-related hearing loss, especially understanding speech-in-noise (SiN) is a major complaint in older adults affected by age-related hearing loss (Anderson, Parbery-Clark, Yi, & Kraus, 2011). Apart from that, this issue might be what affects people most in their daily life since conversation rarely ever take place in spaces devoid of any background noise. The most obvious explanation for the symptoms mentioned above is that they are caused by elevated hearing thresholds. However, this is not the case, as will be elaborated in the next section.

Beyond the treshold

With time evidence has accumulated suggesting that variance in PTA explains, if any at all, only very little of the variance in SiN perception (Cruickshanks et al., 1998; Dubno, Dirks, & Morgan, 1984; Gordon-Salant & Fitzgibbons, 1993; Killion & Niquette, 2000; Souza, Boike, Witherell, & Tremblay, 2007). It therefore is unlikely that the loss of hearing sensitivity is the sole factor contributing to the variety of changes in speech perception in older adulthood.

However, not all facets of speech perception seem to be affected to the same degree by aging. There is evidence that there are differences in the use of temporal speech information within older adults. In particular older adults perform worse in processing the TFS information of the speech signal compared to younger adults (Gordon-Salant & Fitzgibbons, 1999; Gordon-Salant, Yeni-Komshian, & Fitzgibbons, 2010; Gordon-Salant, Yeni-Komshian, Fitzgibbons, & Cohen, 2015; Schneider & Pichora-Fuller, 2001). This does not seem to hold true for TE information, where perception remains more or less stable across the lifespan (Wingfield, Lindfield, & Goodglass, 2000; Wingfield, Wayland, & Stine, 1992). It might have not escaped the readers' attention that this matter might have implications for the AST model (see Chapter 1.1.2), an idea is thus of particular interest and that will be discussed later on (Chapter 1.3.2 and 3.2.1).

Notwithstanding this circumstance, it can be concluded that there are age-related

changes in auditory input due to alterations in the auditory periphery, which in turn, according the remarks of Chapter 1.2.1, would suggest that there might be neuroplastic alterations following these changes.

Another factor that is assumed to be related to speech perception is cognition. In an aim to set a framework for the relation between cognition and speech understanding Rönnberg (2003) proposed a model that the called the ease of language understanding (ELU), which in later years has been refined (Rönnberg et al., 2013; Rönnberg, Rudner, Foo, & Lunner, 2008). In its core the model assumes a relationship between sensory input, information available in long term memory (LTM) and the use of working memory (WM). WM acts as an interface between sensory input and lexical access.

Particularly, if the sensory input does not match any items in the mental lexicon (e.g. because of degraded sensory input), input processing enters an additional processing loop, where phonological and semantic LTM information is used to attempt to restore the input for it to match an item in the mental lexicon. According to the model, this loop is dependent on WM capacity. Thus, the model identifies WM as a key ability for the understanding of language, a view consistent with other works highlighting the importance of WM particularly in older adulthood (Gordon-Salant & Fitzgibbons, 1997).

Similar to hearing sensitivity, age-related changes in cognitive abilities are evident. Generally, aging is accompanied by a decline in cognitive functions. This is evident for fluid abilities, such as speed, reasoning and memory, while at the same time,crystallized skills, such as vocabulary, increase until older adulthood and then remain stable (Salthouse, 2004). Even though there is a debate about the exact trajectories of these declines (e.g. at what age decline starts or how steep it is), there seems to be a consensus that cognitive deterioration in fluid abilities is evident from around 60 years of age (Salthouse, 2009; Schaie, 2009).

Thus, age-related changes in fluid abilities, such as WM, are likely to interact with speech perception in older adulthood. However it should be noted that WM is not the sole cognitive ability that has been suggested to have an influence on spoken language perception in older adulthood. Other cognitive abilities, such as lexical access (Kaandorp, De Groot, Festen, Smits, & Goverts, 2016) or inhibition (K. L. Tremblay, Piskosz, & Souza, 2002)) have been reported to influence speech perception as well. In general it can be stated that cognition is necessary to understand speech and that it is particularly important in older adulthood, either because declining cognitive abilities can hamper speech understanding or because cognition can compensate for impaired sensory input, for example because of elevated hearing thresholds (Anderson et al., 2011; Wingfield, Amichetti, & Lash, 2015; P. C. Wong et al., 2009).

Schuknecht (1964), in his description of neural hearing loss, explicitly restrained the loci of malfunction to lower auditory pathways, but at the same time brought up the hypotheses that higher auditory pathways (i.e. the auditory related cortex and language

relevant areas) might also be susceptible to loss of function contributing to the symptoms of presbycusis.

Indeed, cortical atrophy, as indicated by decreases in volume of gray matter (CV), has been related to peripheral hearing loss (Eckert, Cute, Vaden, Kuchinsky, & Dubno, 2012; Husain et al., 2011; Peelle, Troiani, Grossman, & Wingfield, 2011; Profant et al., 2014). However, it has been argued that it is not hearing loss that is causing this cortical atrophy, but rather, that other factors related to age are the driving factor (Giroud, Hirsiger, et al., 2018; Profant et al., 2014). Following this argument, the brain itself is susceptible to age-related changes and thus might have an influence on speech processing. Consistent with this argumentation, aging has been reported to be accompanied by a general atrophy of the brain (Fjell & Walhovd, 2010; Fjell et al., 2009, 2012; Giroud, Hirsiger, et al., 2018; Hogstrom, Westlye, Walhovd, & Fjell, 2012; Raz et al., 1997; Sowell et al., 2003, for further discussion see Chapter 1.3).

Hence, structural brain age-related brain changes might lead to changes in speech perception.. The idea that changes in brain structure and function can cause difficulties in speech perception has been termed *central hearing loss*, which stands in contrast to *peripheral hearing loss* which relates to extracortical sources of hearing impairments (usually sensory-neural hearing loss), by Humes et al. (2012).

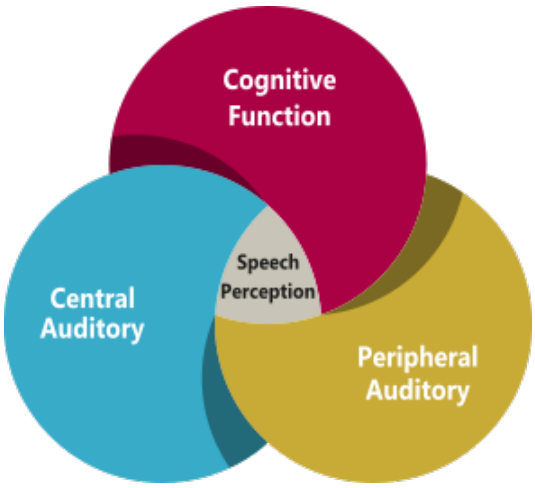

Figure 1.2. Interplay between cognition and central and peripheral auditory factors. Speech perception in older adults is proposed to arise from the interaction between these factors (redrawn after Humes et al., 2012)

Accordingly, these authors argue in favour of a research program for presbycusis, that is based on the assumption that auditory perception and speech communication in older adults are the product of the interplay between cognitive function and central and peripheral auditory factors (see Figure 1.2]).

Intermediate summary

Aging is oftentimes characterized by a loss of sensory function, changes in cognitive abilities and changes of the brain itself. Hence, external (i.e. changes in sensory input) and internal (i.e. changes of the brain) factors that are likely to trigger neuroplastic events are present in older adulthood. Naturally, this has implications on how the brain processes spoken language in older adulthood since different strategies in speech perception due to impaired sensory input or decline in cognitive abilities as well as changes of the brain itself along the lifespan are likely to change the way the brain processes speech.

Of particular interest are speech-in-noise perception, because it is a domain were loss of function is evident in older adulthood and because of its of high relevance for peoples daily life and perception of speech prosody, since this represents an area were function is preserved along the lifespan as well as because of its relation to models of functional neuroanatomy.

In this section it was argued that, because the brain is subject to lifelong changes and because individuals are confronted with a different hearing and language environment (in the sense of changed sensory input and changes within individuals themselves) as they get older, models of language processing should not be generalized to older populations and extensions and refinements of existing models are needed to account for these differences. In the next section, functional and structural peculiarities of the aging brain in general and specific to speech processing will be discussed in more depth.

1.3 Language and the aging brain

After having made the argument that neuronal speech processing is unlikely to be the same between individuals of different ages and highlighting the need for development of speech processing models, functional and structural changes related to aging will be reviewed in this section. In the first part these changes will be discussed on a broader level and then it will be moved on to findings specifically related to speech processing. Based on these models and findings, open questions will be identified and the aims of the studies included in the empirical part (Chapter 2) will be deducted from these open questions.

1.3.1 Structural and functional perspectives on brain aging

Age-related changes in brain structure

Along with the advent of neuroimaging came also new insights into the aging brain. On the structural level it became clear that aging is characterized by atrophy of gray matter in various brain regions (Fjell & Walhovd, 2010; Fjell et al., 2009, 2012; Giroud, Hirsiger,

et al., 2018; Hogstrom et al., 2012; Raz et al., 1997; Raz & Rodrigue, 2006; Sowell et al., 2003). In particular, frontal and temporal regions seem to be affected by cortical atrophy. Early automatic procedures that allowed to acquire observer-independent measures of brain architecture in a timely manner were based on CV (Ashburner & Friston, 2000).

It has later been argued that CV is in fact the product of two other variables, namely cortical surface area (CSA) and cortical thickness (CT) (Panizzon et al., 2009) . In addition CT and CSA have been hypothesized to have different genetic sources (Panizzon et al., 2009) and represent different anatomical properties of the tissue (Rakic, 1988, 1995). According to this view (Eickhoff et al., 2005; Rakic, 1988), CSA reflects the number of cortical columns in a distinct area, while CT is determined by the number and the size of cells within a column, the packing density of the cells, as well as by the number of connections and their myelination. Thus CT and CSA should be considered independent neuroanatomical traits (Meyer, Liem, Hirsiger, Jäncke, & Hänggi, 2014).

In the context of aging especially CT seems to play an important role and has been assumed to be most susceptible to plastic changes along the life-span (Giroud, Hirsiger, et al., 2018; Storsve et al., 2014). Along with atrophy in gray matter a typical finding in older individuals is the loss of white matter integrity and both are assumed to have a detrimental effect on cognitive performance, where a loss of brain structure is associated with a decline in performance (Raz & Rodrigue, 2006). While several risk factors for structural deterioration, such as vascular diseases, stress or hormonal depletion, have been identified, the mechanism responsible for these age-related changes remain largely unclear (Raz & Rodrigue, 2006).

Age-related changes in brain function

On the functional level, a variety of theories and frameworks of age-related changes in brain activation patterns and its influence on behaviour and cognition have been formulated based on recent findings. Among these findings, one that has spurred the development of theories, is that older adults have been observed to show a bilateral pattern of functional activation where younger adults show unilateral activation (e.g. Cabeza et al., 1997; Grady et al., 1994; Nielson, Langenecker, & Garavan, 2002; Reuter-Lorenz et al., 2000; Stebbins et al., 2002). These findings have prompted Cabeza (2002) to formulate a model in which this phenomenon reflects general aging processes. In what is called the Hemispheric Asymmetry Reduction in Older Adults (HAROLD) model, it is suggested that prefrontal cortex (PFC) activation is less lateralized in older than in younger adults under similar circumstances. Within the HAROLD model, reduced hemispheric asymmetry is assumed to be most likely an effect of a compensation effort of the brain (Cabeza et al., 1997).

Another observation, related to differences between age groups, is that older adults showed greater activation in prefrontal regions, while at the same time showing reduced

activation in anterior regions (e.g. Grady et al., 1994; Grossman et al., 2002; Madden et al., 2002). Similar to the HAROLD model this has been taken as a general principle of work of the aging brain and has been called the Posterior Anterior Shift in Aging (PASA, Davis, Dennis, Daselaar, Fleck, and Cabeza (2007)). This phenomenon has also been interpreted from a compensation viewpoint, where frontal areas compensate for a loss of function in other areas. According to the proponents of the theory, posterior regions in the brain show declines in neural processing which then can be compensated by allocating neural resources in frontal regions.

Hence, both the HAROLD and the PASA model interpret age-related changes as the manifestation of a compensation effort due to cognitive/processing declines in older adulthood. However, the idea of the PFC as the locus of compensation efforts is contradicted by findings from structural imaging, which show the the PFC to be most susceptible to age-related cortical atrophy (e.g Fjell & Walhovd, 2010). Further, increased activation in older adults occurs not exclusively in posterior but also in anterior regions (D. C. Park & Reuter-Lorenz, 2009). From that perspective it appears to be unlikely that the PFC is a compensatory hub in the aging brain.

A more general interpretation of findings, such as those mentioned above, is given by the Compensation-Related utilization of Neural Circuits Hypothesis (CRUNCH, Reuter-Lorenz and Cappell (2008)). In this account, older adults are assumed to show general overactivation of the brain compared to younger adults. Reuter-Lorenz and Cappell (2008) argue that this overactivation in older adults is beneficial for older adults' performance, representing allocation of additional neural resources. According to the hypothesis, older adults depend on higher levels of activation to achieve the same level of performance than younger counterparts. This implies that, for lower levels of task demands, performance levels equal to younger adults can be attained because sufficient additional neural resources can be recruited while for higher levels of task demands older adults performance falls behind younger adults because resources have already been exhausted.

Beyond compensation

In addition to functional and structural neural influences on cognition the Scaffolding Theory of Aging and Cognition (STAC, D. C. Park and Reuter-Lorenz (2009); Reuter-Lorenz and Park (2014)) hypothesis also incorporates life-course factors into its model. The STAC model explicitly identifies functional and structural challenges that occur in older adulthood. Structural challenges refer to cortical thinning, regional atrophy, loss of white matter integrity and dopamine depletion and functional challenges refer to maladaptive, age-related patterns of brain activity. According to the STAC-model these challenges are predictive of the cognitive functioning of an individual.

Maladaptive changes can be counteracted by what is called 'compensatory scaffold-

ing'. Compensatory scaffolding describes different neural compensation strategies, such as recruitment of additional neural resources. The hypothesis states that this scaffolding can be enhanced by various lifestyle activities such as exercise or intellectual engagement. In the revised version of the hypothesis (Reuter-Lorenz & Park, 2014) the STAC-r model came to include life-span and life-course factors.

In other words, it is assumed that, apart from genetic factors, experiences that have been made during the lifespan influence brain structure and function and ultimately the level and rate of cognitive change in older adulthood and factors such as education and physical fitness are thought to be beneficial for neural function and structure while others, such as, stress or depression are assumed to be harmful. This model thus represents a comprehensive framework of how structure and function change with advancing age.

The HAROLD, PASA and CHRUNCH models attribute differences in neural functioning to compensation processes. However, this does not necessarily have to be the case. An alternative explanation for differences in neural activation is that these reflect a *dedifferentiation* phenomenon. This term was originally used to describe higher correlations found between different cognitive measures within older individuals as compared to younger adults and was then extended to neural functioning (Baltes & Lindenberger, 1997; S.-C. Li et al., 2004).

In the case of neural functioning, dedifferentiation means that neural responses to stimuli lose their regional specificity. In other words, neural processing that is strongly restricted to specific cortical areas in younger individuals, might be more widely distributed in older adults. Within this framework it is hypothesized that this loss of specificity is due to an increased signal-to-noise ratio (SNR) in older adults likely due to a decline of the dopaminergic system (S.-C. Li, Lindenberger, & Sikström, 2001a). Thus, phenomena like reduction in asymmetric processing could also be interpreted as an effect of dedifferentiation (Cabeza, 2002). In this case, less lateralization would indicate a loss of specificity, that would be unilateral processing and thus not be a consequence of a compensation effort but of neural dedifferentiation. In contrast to neural compensation, neural dedifferentiation would lead to worse performance.

Intermediate summary

Age-related brain changes are evident on the structural and the functional level. While neuroanatomical decline is related to behavioural deterioration, the relationship between brain activation and performance is less clear. In particular, some authors interpret activation patterns from a compensatory point of view while others hypothesize that altered neural activation is due deficient processing, such as neural dedifferentiation.

Some models, such as the HAROLD and the PASA model make specific predictions about specific differences in neural activation patterns while others, such as the CRUNCH or STAC(-r), entertain a more holistic approach, considering a range of factors potentially

influencing neural processing over the lifespan.

In general, the aforementioned frameworks illustrate that brain function and structure in older adults differ from those of younger individuals, presumably due to either intrinsic or extrinsic changes of the brain. This gives further support to the argument that models of speech perception need to account for these changes.

1.3.2 Speech processing in the aging brain: current views and open questions

After having reviewed structural and functional changes in the brain related to aging on a more general level, changes of neural functioning and brain anatomy and their specific influence on speech perception will be discussed in the following. Open questions will be highlighted and the hypotheses for the empirical part (Chapter 2) will be deduced along with a brief mention of the methods and results of the corresponding study.

As has been pointed out in Section 1.2.2 there is evidence that TE and TFS show different lifespan trajectories, where TFS processing is more susceptible to declines related to aging Gordon-Salant and Fitzgibbons (1999); Gordon-Salant et al. (2010, 2015); Schneider and Pichora-Fuller (2001). Evidence for a neural reasons for this processing deficits come from (Anderson, Parbery-Clark, White-Schwoch, & Kraus, 2012). They recorded auditory brainstem responses (ARB) to speech syllables in younger and older participants. Results demonstrated that compared to younger adults, older adults showed delayed responses to rapidly changing formant transitions of the syllable. Accordingly, the authors suggested that a loss of temporal precision in subcortical auditory nuclei accounts for difficulties in TFS processing experienced by older adults.

Similar to this, Grose, Mamo, and Hall III (2009) reported that the auditory steady state responses (ASSR) were significantly different between older and younger adults for sinusoidally modulated tones with a modulation frequency of 128 Hz. For a lower modulation frequency of 32 Hz however, no age effect was evident. This results speak to the idea that older adults show timing deficits mainly for high-frequency modulated acoustic input. Further evidence for temporal processing differences between TE and TFS in ASSR is provided by Goossens, Vercammen, Wouters, and Wieringen (2016). They report that ASSR in the θ frequency range were larger for in an older group than in a middle-aged and a young group. Neural oscillations in the θ range are assumed to reflect TE or prosodic processing (Doelling et al., 2014; Giraud & Poeppel, 2012; Poeppel, 2001, 2003, see Section 1.1.2).

Thus, there is evidence that older adults' neural processing of auditory temporal information is particularly sensitive to prosodic cues on the sub-lexical level, mirroring evidence from behavioural research (Wingfield et al., 2000, 1992). While these findings focus on auditory processing on the syllabic level or apply non-speech stimuli, little is

known about neural processing of prosodic cues on the word or sentence level in older adults.

Study I: Aims and hypotheses

The main aim of the *Study I* (Giroud et al., n.d., in preparation, see Chapter 2.1.6) was to investigate neural mechanism of prosody perception in older adults on the word level. In a mismatch negativity (MMN) EEG paradigm, neural responses to word-stress pattern were measured in an old and a young group. In line with the research discussed above, it was hypothesized that MMN magnitudes are similar between older and younger adults. In addition, T1-weighted MR images were recorded to measure brain atrophy. Analogous to the notion of age-related central hearing loss, it was hypothesized that cortical atrophy would be detrimentally related to speech perception performance.

Results showed that there were differences between age groups in MMN magnitudes in response to word stress. Moreover, it was the older group whose MMN magnitudes were larger. This extends previous results reporting increased sensitivity to prosodic cues in older adults to the word level. Within the older group, individuals with less cortical atrophy, in particular in right hemispheric areas, performed better in a prosody perception task. In accordance with previous research, this finding highlights the importance of central factors of hearing loss, also in the case of perception of prosodic cues.

One insight from (Giroud et al., n.d., in preparation) is that cortical atrophy can have a negative effect on speech perception. This finding is reflecting other work (Giroud, Hirsiger, et al., 2018; P. C. Wong, Ettlinger, Sheppard, Gunasekera, & Dhar, 2010) that demonstrates loss of performance related to cortical thinning (but not to differences in CSA). Giroud, Hirsiger, et al. (2018) investigated the relationship between several measures of supra-threshold (i.e. independent from hearing thresholds) auditory perception and CT and CSA in different auditory ROIs. The set of supra-threshold tests consisted of a test for frequency selectivity (FS) and temporal compression (TC) (Lecluyse, Tan, McFerran, & Meddis, 2013) and a measure of SiN perception (Wagener, Brand, & Kollmeier, 1999a, 1999b, 1999c). FS and TC can be broadly described as measures of frequency (FS) and temporal (TC) resolution of the central auditory system. For these measures, cortical thickness in different auditory areas (i.e. PT and Heschl's sulcus (HS)) significantly predicted performance scores, i.e. thicker cortices were related to better performance.

Difficulties in understanding speech in the presence of background noise is one of the major complaints within older individuals and is experienced even in the absence of peripheral hearing loss (see Chapter 1.2.2). Investigating potential causes of this adversity is particularly imperative since it has far-reaching impacts on individuals real-life. Giroud, Hirsiger, et al. (2018) found that also for this measure cortical atrophy was

predicting performance in a SiN test in older adults. Two regions, right hemispheric HS and right hemispheric pars orbitalis (POR) of the IFG, turned out to be of particular importance. While the HS is usually considered to be part of the PAC, the POR is part of the IFG to which usually higher-level language functions are attributed (see Chapter 1.1.2). Thus, the interpretation of the results was that central hearing loss in primary and higher level auditory related areas is contributing to the difficulties in SiN perception observed in older adults.

However, a earlier study which was investigating the same relationship found slightly diverging results (P. C. Wong et al., 2010). While they also found anatomical measures (i.e. CV) of regions within the IFG (i.e. pars triangularis (PTRI) to be related with performance in SiN perception, they did not find this relationship for primary auditory regions. Instead, they reported that cortical thickness in the left superior frontal gyrus (SFG) did significantly predict SiN performance. The SFG has usually been related to cognitive processes such as WM (Awh, Smith, & Jonides, 1995; Boisgueheneuc et al., 2006; Braver et al., 1997; Cornette, Dupont, Salmon, & Orban, 2001) and not to the core language network.

Thus, one question is how these different results came to be and what they mean in terms of the relationship between SiN perception and central auditory factors.

Study II: Aims and hypotheses

The main aim of the *Study II* (Keller, Giroud, & Meyer, n.d., in preparation, see Chapter 2.2.6) was to contribute to the clarification of the relationship between elementary and higher-level language processing, cognition and SiN perception based on neuroanatomical relationships. Using a whole-brain approach, correlations between anatomical measures (CT and CSA) and SiN performance scores within a group of older adults with mild hearing loss and younger normal hearing participants were calculated. Significant clusters from this analysis were further subjected to a multiple regression analysis including interaction effects between anatomical measures and age-group, to elucidate which regions are particularly important for older adults. It was hypothesized that primary, secondary and cognition related regions show a significant relationship with SiN.

In addition, several cognitive abilities within the older group were measured to investigate the relationship between cognition and SiN. For this analysis it was expected that cognitive abilities would interact with the relationship between anatomical measures and SiN in regions related to cognition.

Results confirmed that CT of several primary and secondary auditory regions significantly predicted SiN. Notably, the left SFG was found to be a significant predictor of SiN and seemed to be particularly important for the older group. This relationship was modulated by WM abilities, indicating that the relationship between CT in SFG was stronger for participants with better WM. Thus, results from previous studies were

successfully replicated. Moreover, these results suggest a potential explanation for the diverging results from previous studies.

The main issue outlined in the course of this text was that models of the functional neuroanatomy of speech perception are unlikely to be able to account for speech processing across the lifespan. Among these models, the AST model represents an elegant proposal aiming at bridging the gap between linguistics and neuroscience (Poeppel, 2001, 2003; Poeppel & Embick, 2005, see Chapter 1.1.2). Initial evidence for a different processing of the acoustic core components of the model, that is TE and TFS, by younger and older adults, has been highlighted by the investigation of neurophysiological responses to TE and TFS (Anderson et al., 2012; Goossens et al., 2016; Grose et al., 2009). However, a prediction that is being made by the AST model concerns localization of cortical sources of TE and TFS processing. The AST framework assumes a lateralized processing for either type of temporal speech information and predicts left hemispheric asymmetry for TFS processing and right hemispheric asymmetry for TE processing.

One of the main observations of neurofunctional processing in older adults is that asymmetries are often times reduced (Cabeza, 2002; Reuter-Lorenz & Park, 2014). This phenomenon has also been observed in speech processing. Bellis, Nicol, and Kraus (2000) reported that in older participants, in contrast to younger adults and children, early neurophysiological components of speech perception were symmetrically distributed over hemispheres. Along the same lines, Goossens et al. (2016) report that θ-oscillations related to TE processing were processed in a symmetrical manner by older adults. However, these results are based on EEG recordings, which have a low spatial resolution and it is thus difficult to infer on the underlying anatomical source giving rise to this pattern.

The AST hypothesis makes specific predictions about where in the brain asymmetries in spectrotemporal processing are located, namely in early and secondary regions. It is thus not clear from these investigations, whether the reduced asymmetries observed in older adults are due to changes in the lateralization pattern of these specific regions.

Further, a classification of these results within frameworks of cortical aging is missing. In other words, it remained unclear whether symmetrical processing is a consequence of compensation efforts or neural dedifferentiation (see Chapter 1.3.1). Lastly, there was no relationship established between cortical atrophy and the activation patterns. Hence, it was unclear so far, whether these age-specific patterns were solely of a functional nature or whether they might be related to structural changes occuring in older adulthood.

Study III: Aims and hypotheses The main aim of the *Study III* (Keller, Neuschwander, & Meyer, n.d., submitted for publication, see Chapter 2.3.9) was to test the predictions made by the AST hypothesis in terms of lateralization in older adults. A second

aim was to establish, if reductions in asymmetry were evident, whether a decrease in lateralization is likely to be a compensation effort or whether it might be the effect of neural dedifferentiation. Thirdly, the study aimed at describing potential relationships between activation patterns and brain anatomy.

A group of older adults underwent functional and structural MRI testing using a paradigm established in younger adults by Liem et al. (2014), showing lateralization in posterior superior temporal regions, including the PT, in response to suprasegmental manipulations on the sentence level as predicted by the AST model. Based on previous observations from speech processing and other domains it was hypothesized that older adults would show bilateral patterns of processing in response to the manipulation. It was expected that this was a consequence of neural dedifferentiation evident in a relationship between variability in lateralization responses and speech perception performance and not a compensation effort which would be seen in a relationship between absolute lateralization and performance. In line with work suggesting a detrimental effect of cortical atrophy (e.g. Giroud, Hirsiger, et al., 2018; Keller, Giroud, & Meyer, n.d.; P. C. Wong et al., 2010) it was hypothesized that thinner cortices would be related to more neural dedifferentiation.

Indeed, the obtained results confirmed the hypothesis of reduced lateralization in older adults. The relation between performance and activation patterns provided evidence for a cruical role of neural dedifferentiation in the loss of hemispheric specialization.

Chapter 2

Empirical part

2.1 Article I: Atrophy in auditory-related brain circuits but still good auditory perception in older adults? Bridging the structure-function-behavior gap using a word stress discrimination paradigm.

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A similar version of this manuscript is currently in preparation for submission

Abstract Age-related hearing loss is one of the top three causes of disability in older adults. Due to the related decline in speech perception, age-related hearing loss may yield difficulties for older adults to partake in spoken conversations and subsequently lead to social isolation. In order to avoid such consequences, it is necessary to better understand the mechanisms behind age-related changes in speech perception such as the decline in perception of spectral speech cues. The purpose of this study was to evaluate to what extent a decline in spectral speech discrimination in older adults can be explained by atrophy in cortical auditory areas (i.e. central hearing loss). Yet, it has been suggested that older adults may still be sensitive to spectral speech cues marking prosodic events, while the neural mechanisms behind this finding have not yet been addressed. We used an MMN experiment to evaluate sensitivity to word stress patterns in younger and older adults with normal audiograms. The German word /Hubschrauber/ with a stress on the first syllable was presented as the standard stimulus, while the same word with a) a stress on the second syllable and b) on the third syllable was used as deviants. In a behavioral discrimination task, participants evaluated different levels of stress (i.e., 20, 30, and 40 Hz pitch differences) on each syllable of the same word as used in the MMN experiment. Furthermore, in order to objectively assess central age-related hearing loss, we obtained T1-weighted MR images from all participants and used surface-based morphometry to compute cortical thickness and cortical surface area in left and right auditory areas. Our results show that older adults performed worse in the pitch discrimination task than younger adults while also showing lower cortical thickness in auditory regions. Within the older groups, individuals with more pronounces atrophy in right auditory areas performed worse than those who had less atrophy. Yet, the MMN experiment revealed that older adults were more sensitive to word stress than younger adults and that larger cortical surface area in left auditory areas related to higher word stress sensitivity. We propose that describing the neural mechanisms behind age-related changes in the sensitivity to speech cues may help to develop novel rehabilitation strategies for older adults with central age-related hearing loss.

2.1.1 Introduction

A majority of older adults who have age-related hearing loss show poorer performance in speech perception in noise (Helfer & Wilber, 1990; Zekveld, Kramer, & Festen, 2011), in speech perception in babble noise (Dubno et al., 1984) as well as in perception of time compressed speech (Gordon-Salant & J, 2001) as compared to individuals with normal-for-age hearing. Mediated by the difficulty to understand speech, age-related hearing loss may therefore reduce the frequency to which older adults partake in spoken conversations (Heinrich, Henshaw, & Ferguson, 2015; Vannson et al., 2015). Yet, difficulties to engage in spoken communication have been shown to cause social isolation, higher rates of depressive symptoms as well as lower quality of life (Arlinger, 2003; Heinrich et al., 2015; Vannson et al., 2015). Consequently, age-related hearing loss is one of the top three leading causes of disability in older adults (Organization, 2008) and affects approximately 30% of older adults at the age of 65 years and older (Homans et al., 2017) and approximately 50% of older adults above the age of 80 years (Roth et al., 2011).

Meanwhile, research has reported that older adults with normal-for-age hearing also show lower speech perception performance in various tasks as compared to younger adults, for example in speech in noise tasks (Giroud, Hirsiger, et al., 2018; Helfer & Wilber, 1990), in speech in babble noise tasks (Dubno et al., 1984), in time compressed speech perception tasks (Gordon-Salant & Fitzgibbons, 1993), in gap detection tasks (Harris, Eckert, Ahlstrom, & Dubno, 2010), in temporal order discrimination tasks (Fogerty, Humes, & Kewley-Port, 2010; Fogerty, Kewley-Port, & Humes, 2012), as well as in fricative discrimination tasks (Giroud, Lemke, et al., 2018). Thus, age-related decline in speech perception may not only be caused by age-related hearing loss which typically refers to an age-related decline in inner ear functions (=peripheral age-related hearing loss) and is usually measured by the audiogram (Pickles, 2012), but has also been associated with central age-related hearing loss (Humes et al., 2012). Central age-related hearing loss occurs as a function of age-related decline in auditory brain circuits (Giroud, Hirsiger, et al., 2018) as well as cognitive decline in older adults (Humes et al., 2012) and may lead to speech perception difficulties in older individuals independently of elevated audibility thresholds in the audiogram (Giroud, Hirsiger, et al., 2018).

Even though most of the research comparing older adults with age-appropriate peripheral hearing to younger adults suggest that older adults perform worse in speech perception, it has also been shown that older adults may still be sensitive to prosodic speech cues to a similar extent as younger adults (Wingfield et al., 2000, 1992). For example, sentence recall has been shown to be better when prosodic cues are presented in line with the syntactic structure as compared to when syntax and prosody are placed in conflict, and this effect has been demonstrated to be larger in peripherally normal hear-

ing older compared to younger adults (Wingfield et al., 1992). Furthermore, recognition of words with no segmental information has been shown to be facilitated to the same degree in younger and older adults when prosodic cues indicated the number of syllables and syllabic stress (Wingfield et al., 2000). Initial electrophysiological data assessing the N400 and the P600 have further supported this evidence by revealing that older adults integrate prosodic information in real-time during resolving early and late closure ambiguities (Steinhauer, Abada, Pauker, Itzhak, & Baum, 2010). In sum, research suggests that even though peripherally normal hearing older adults show considerable age-related decline in various speech perception tasks, they rely on prosody and use word stress to improve speech perception to the same extent as younger adults do.

Investigating age-related differences in the extent to which individuals use speech parameters such as prosody (i.e. word stress) for improving speech perception may therefore be particularly fruitful in order to develop novel rehabilitation strategies for older adults with central age-related hearing loss. Importantly, since most of the rehabilitation research targets older adults who have elevated audibility thresholds, many older adults who experience central age-related hearing loss and who have normal-for-age audiograms will not get professional help even though the severity of the consequences can be expected to be similar. Yet, there is a lack of studies investigating age-related changes in the perception of different speech parameters, particularly those which may not be affected by aging and which may serve as compensatory for other cues which have been shown to be more difficult to perceive in old age, for instance fricatives and other phonemes (Giroud, Lemke, Reich, Matthes, & Meyer, 2017). However, such research is needed in order to develop advanced rehabilitation interventions for improving speech perception in older adults with normal audiograms and avoid the drastic consequences of untreated hearing loss. To address this need, we used a word stress discrimination paradigm in order to assess the sensitivity to word stress in older adults and younger controls with age-appropriate peripheral hearing. Crucially, sensitivity to acoustic cues does not always directly translate into behavior (Steinhauer et al., 2010) which is why we used more fine-graded indicators of auditory sensitivity to word stress. We therefore also recorded the mismatch negativity (MMN) to study auditory functional sensitivity to word stress in more depth. To the best of our knowledge, this is the first study to investigate age-related differences in word stress perception combining behavior and EEG.

Furthermore, in order to elucidate the relation between behavioral and neurofunctional word stress perception and age-related central hearing loss, we objectively assessed central age-related hearing loss by computing cortical thickness (CT) and cortical surface area (CSA) from T1-weigthed MRI images in six bilateral auditory regions and thereby quantified the atrophy in auditory-related brain circuits, a strategy proposed just recently (Giroud, Hirsiger, et al., 2018). Moreover, investigating CT and CSA separately allows

to disentangle different aspects of cortical structure as CT and CSA have been described to have no genetic relationship (Rakic, 1988, 1995, 2007), and only CT has been shown to reflect modulations as a result of training or experience (Bermudez, Lerch, Evans, & Zatorre, 2008; Engvig et al., 2010). In other words, age-related central hearing loss which has manifested in auditory-related areas of the brain is expected to be driven by a decline in CT, while CSA is hypothesized to be more strongly intertwined with genetically determined characteristics of auditory perception (Giroud, Hirsiger, et al., 2018; Meyer et al., 2014; Pontious, Kowalczyk, Englund, & Hevner, 2008).

In sum, we combined behavior, neurofunctional and neurostructural data to investigate the relation between genetically determined as well as experience-driven factors of central age-related hearing loss and the perception of prosodic speech cues, namely word stress, in younger and older adults with normal peripheral hearing. In addition to computing CT and CSA of auditory-related brain circuits and assessing behavioral sensitivity to word stress, we collected MMN data evoked by word stress variations. Accordingly, we used a passive oddball paradigm and presented the German word /Hubschrauber/, which has inherently a stress on the first syllable, and systematically moved the stress position to the second and third syllable while recording the MMN time-locked to each syllable. In general, we expected to find a larger MMN to a stress on the third syllable compared to the second syllable as a function of top-down control as this is less common in German than a stress on the second syllable in three-syllabic words (Janßen, 2004; Jessen, Marasek, Schneider, & Classen, 1995). Furthermore, as a function of bottom-up acoustic processing, we expected the MMN to occur time-locked to all syllables where an acoustic difference between the standard stimulus and the deviant stimulus occurred (see Table 1 for detailed hypotheses). Also, assuming that older adults are sensitive to word stress to the same extent as younger adults, we expected them to evoke similar MMN magnitudes.

2.1.2 Materials and Methods

Participants

In this study, 23 healthy older adults (OA) (age range = 67-84 years, Mage = 72.39 years, 11 females) and 15 younger controls (YA) (age range = 20-29 years, Mage = 24.33 years, 12 females) were compared. All older participants scored above 26 points in the Mini-Mental State Examination (MMSE) (Folstein, Folstein, & McHugh, 1975). Furthermore, participants reported that there was no past or present neurological, psychiatric, or ear disease. Also, no ear or brain surgery was performed in the past. Furthermore, they denied suffering from any language or hearing disorder such as tinnitus, sensorineural hearing loss or dyslexia. In addition, all participants were native speakers of (Swiss-) German, right-handed as assessed by the Annett Hand Preference Questionnaire (Annett,

1970), did not practice more than six hours of music per week, and were not bilinguals in terms of that they did not learn a second language in preschool age. All participants passed the safety requirements for MRI scanning in order to obtain a T1-weighted MR image, which was recorded for a previous study (Giroud, Hirsiger, et al., 2018).

Only participants with age adequate peripheral hearing were included in this study. According to the World Health Organization (WHO) a pure-tone average (PTA) of 25 dB or less for frequencies 500, 1000, 2000, and 4000 Hz is graded as "no impairment", while a PTA between 26 and 40 dB is rated as a "slight impairment" in the hearing impairment grading scale. Correspondingly, in this study we only included older adults with a PTA smaller than 30 dB to ensure that the stimulus material is audible for each participant and that the PTA does not imply a hearing loss that would be diagnosed in a clinic. Furthermore, only participants with symmetrical hearing (no more than 15 dB difference between left and right ear) were included in this study. PTA was assessed using a probe-detection paradigm with pure tones presented for 16 ms and 250 ms at 500, 1000, 2000, and 4000 Hz which were averaged after the procedure. Even though we used a conservative inclusion criterion for the peripheral hearing, there was a significant difference between the two age groups in the PTA ($t(37)=-1.71$, $p=.048$, 1-tailed). The audiograms of the YA and the OA group of this study are depicted in Figure 2.1.

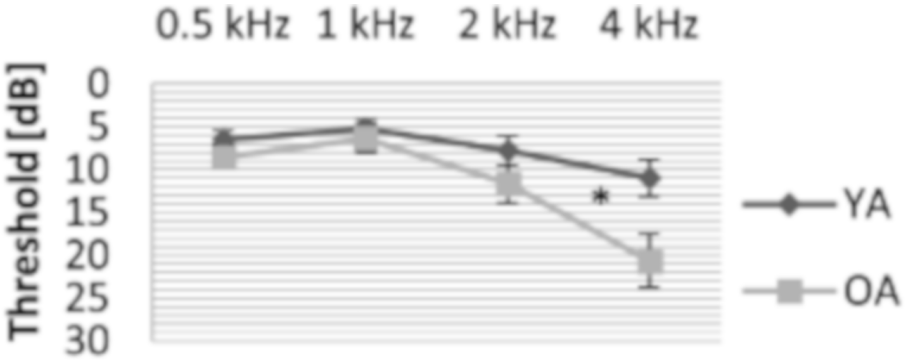

Figure 2.1. This Figure shows the pure-tone thresholds separately for the younger (YA) and the older adults (OA). Both groups can be considered as normal hearing, even though they differ in their pure-tone average.

The local ethics committee of the Canton Zurich approved the study, and written informed consent was obtained from all participants. Participants were paid for their participation.

Stimulus material

The German word /Hubschrauber/ (English: helicopter) was recorded at a sampling rate of 44.1 kHz by a professional female speaker at the Phonetics Laboratory of the University of Zurich. The speaker was instructed to produce three versions of the word

/Hubschrauber/, one with a stress on the first syllable, one with a stress on the second syllable and one with a stress on the last syllable. The realization of syllable stress involved a manipulation of the fundamental frequency F0, which has been shown to be a relevant cue to mark stress in the German language, while a word stress on the initial syllable is most common (Jessen et al., 1995). For each of the three syllables of the word /Hubschrauber/, a stressed and an unstressed version was then segmented for subsequent stimulus manipulation. This was performed using Praat software (version 5.3.68, available here: http://www.fon.hum.uva.nl/praat/). All of the segmented files were first normalized to 72 dB and the duration was equalized between similar syllables. Furthermore, in order to create a stressed and an unstressed version of each syllable of the word /Hubschrauber/, which only differed in the pitch contour while all other parameters (duration, amplitude, frequencies) were kept constant, the stressed pitch contour was extracted for each syllable. Subsequently, for each unstressed syllable a version was created in which the extracted stressed syllable contour replaced the unstressed contour. This procedure resulted in 6 syllables, an unstressed and a stressed version of each of the three syllables of the word /Hubschrauber/ in which all other parameters except the pitch contour were kept constant. After, all the syllables were combined into three versions of the word /Hubschrauber/ (see Table 2.1 and Figure 2.2): First, one version consisted of the word with a stress on the first syllable, but no stress on the second and third syllable. This stimulus was used as the standard stimulus in the mismatch negativity experiment, because it contains the typical German pronunciation of the word /Hubschrauber/. Second, a version with a stress on the second syllable, but no stress on the first or third syllable was used as Deviant 1 in the mismatch negativity experiment. Third, the version with a stress on the third syllable, but no stress on the first or second syllable was used as Deviant 2 in the mismatch negativity experiment. In addition, for the behavioral task only, for each of these three stimuli three other versions were created in which the pitch on the stressed syllable was shifted up 20 Hz, 30 Hz, and 40 Hz.

Table 2.1

This table shows the pitch of each syllable of the three versions of the word Hubschrauber used for the mismatch negativity experiment. In addition, in the bottom, the predictions about the occurrence of the mismatch negativity (MMN) based on these pitch differences are described.

	Syllable 1	Syllable 2	Syllable 3
Standard stimulus	238.53 Hz	173.91 Hz	169.67 Hz
Deviant 1	220.48 Hz	246.91 Hz	169.67 Hz
Deviant 2	220.48 Hz	173.91 Hz	223.21 Hz
Hypotheses	Time-locked to Syllable 1, a MMN should occur in both deviants	Time-locked to Syllable 2, a MMN should only occur in Deviant 1	Time-locked to Syllable 3, a MMN should only occur in Deviant 2

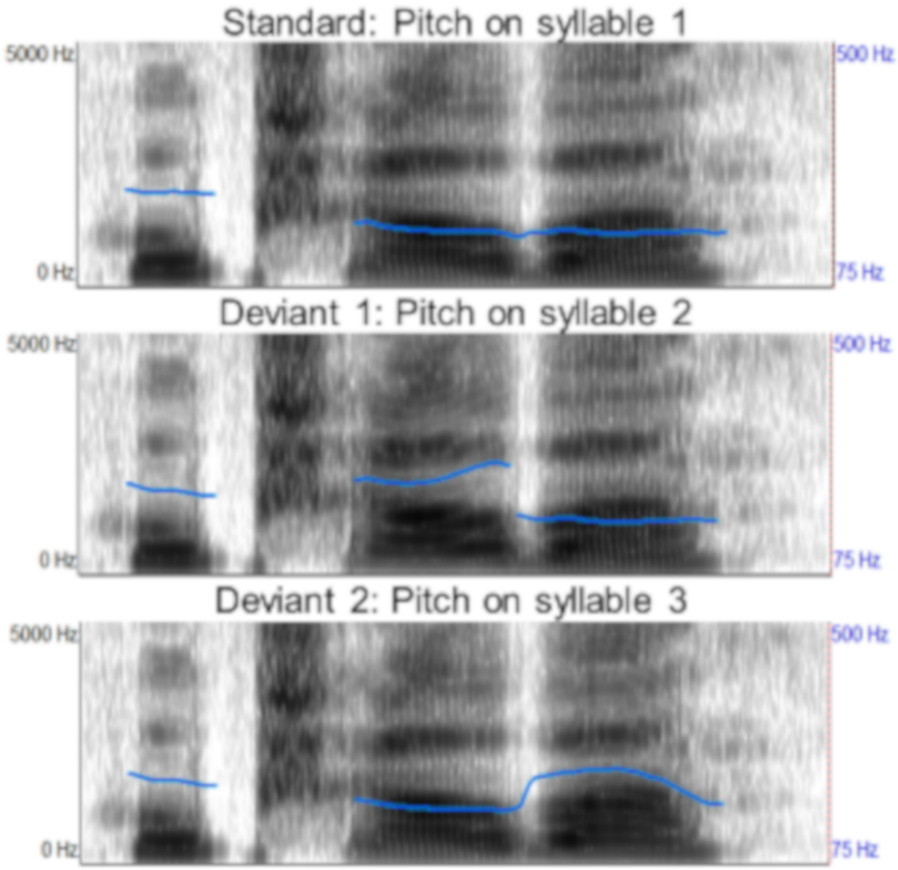

Figure 2.2. Figure 2.2 depicts the spectrogram of the three stimuli consisting of the German word /Hubschrauber/ with three different word stress patterns used for the mismatch negativity experiment. On the top, the standard stimulus is shown with a stress on the first syllable. In the middle, the Deviant 1 with a stress on the second syllable is depicted, while on the bottom the Deviant 2 with a stress on the third syllable is shown. The left axis represents the scaling for the stimulus spectrum, while the right axis (in blue) shows the pitch contour indicating the different stress patterns of the three stimulus versions.

Brain Function: Mismatch negativity

We used a standard passive oddball procedure to evoke the mismatch negativity (MMN) (Näätänen, Paavilainen, Rinne, & Alho, 2007). Participants were seated in a comfortable chair at a distance of about 1 m in front of a screen, which played a silent movie without arousing content. Participants were instructed not to pay attention to the auditory stimuli. Presentation software (www.neurobs.com; version 14.9) controlled the experiment and presented the stimulus material at 72 dB SPL via in-ear headphones (Sennheiser CX271). The standard stimulus was presented 488 times (p=0.75), while each of the two deviant stimuli was presented 81 times (each p=0.125) in a randomized order with a jittered inter-stimulus interval of 1000 ms. EEG was continuously recorded using a 128 electrode system (BioSemi AcitveTwo, Amsterdam, Netherlands) with a

sampling rate of 512 Hz, online references CMS/DRL, and with online bandpass filter between 0.1-100 Hz. Impedances were kept below 30kΩ. Brain Vision Analyzer Software (Version 2.1.0, Brainproducts, Munich, Germany) was used for preprocessing the data. The data was offline bandpass filtered between 0.1-80 Hz using a notch filter. After, an independent component (ICA) analysis was applied to remove eye movements (Jung et al., 2000). Noisy channels were interpolated (Perrin, Pernier, Bertnard, Giard, & Echallier, 1987) using topographic interpolation (order: 4, degree: 10, lambda: 1E-05) and movement artifacts were removed with a semi-automatic raw data inspection (maximal voltage step 50μV/ms, maximal difference in 200 ms intervals of 200 μV). The data was then re-referenced to linked left and right mastoid and a narrower bandpass filter from 0.1-20 Hz (12dB/oct) was applied. Furthermore, the data was segmented into -200-2000 ms segments time-locked to stimulus onset and baseline corrected with regard to the pre-stimulus interval (see Figure 2.3). For each participant, the average of the standard stimuli, the Deviant 1 stimuli and the Deviant 2 stimuli was then calculated. Additionally, in order to perform peak amplitude detection, the MMNs were extracted time-locked with -100-600ms with respect to each syllable and baseline corrected for the 100ms pre-syllable interval. This baseline correction for the signal time-locked to each syllable was crucial, as we expected to find differences within these baseline intervals between subjects as a result of the MMNs occurring in these time intervals which might influence the subsequent MMNs. For electrode Cz, amplitude peak detection was applied for the global negative maxima time-locked to Syllable 1 within 200-400 ms after stimulus onset (Syllable 1), time-locked to Syllable 2 within 100-300 ms (Syllable 2), and time-locked to Syllable 3 within 100-300 ms (Syllable 3) after syllable onset. Peak amplitude in an interval of +/- 10 ms around peak was exported with respective peak latency for each participant separately for each MMN resulting in nine peak amplitudes and respective latencies for each participant, namely for the standard stimulus, the Deviant 1 and the Deviant 2 for each syllable (Syllable 1, Syllable 2, and Syllable 3) respectively.

Behavior: Word stress perception

After performing the passive MMN experiment, participants completed a word stress discrimination task in order to evaluate discrimination accuracy of the stimulus material used in the MMN experiment. Participants were instructed to press a button in a forced choice experiment and indicate whether a pair of two words were the same or different by clicking the left mouse button for same and the right mouse button if the words were perceived as different. Word pairs consisted of the same three stimuli used for the MMN experiment, and in addition of the same words differing in pitch (pitch shift 20, 30, or 40 Hz). In total, 72 trials were randomly presented consisting of 36 trials with equal stimuli in a pair and 36 trials with different stimuli in a pair. The interval between the two words of a word pair was set to 200 ms, while the next trial started 700 ms after an

answer of the participant was registered. We compared discrimination accuracy between the two age groups for word pairs with a difference in stress position, or a difference of 20 Hz, 30 Hz, or 40 Hz in stress separately for each syllable of the word /Hubschrauber/.

Brain Structure: Cortical thickness and mean surface area

Two high resolution T1-weighted images were obtained for each participant from a 3.0 T Philips Ingenia scanner (Philips Medical Systems, Best, The Netherlands) with a 12 channel head-coil using an anatomical 3D Turbo-Field-Echo (TFE) sequence with echo time (TE) = 3.79 ms, repetition time (TR) = 8.18 ms, field of view (FOV) = 240 x 160 x 240 mm, acquisition matrix = 256 x 256, 160 slices per volume, and isotropic voxel size = 0.94 x 0.94 x 1 mm, flip angle (α) = 90°. For four older participants, only one T1-weighted image was acquired. In order to create a single image volume with high contrast-to-noise, the two obtained T1-weighted images were averaged for all other participants (Reuter, Rosas, & Fischl, 2010). FreeSurfer image analysis suite (version 5.1.0.), which is documented online (http://freesurfer.net/), was used for cortical surface reconstruction. Several preprocessing steps for surface-based morphometry (SBM) as implemented in the FreeSurfer pipeline were calculated in a fully automated way (Dale, Fischl, & Sereno, 1999; Dale & Sereno, 1993; Fischl, Liu, & Dale, 2001; Fischl et al., 2002; Fischl, Salat, et al., 2004; Fischl, Sereno, & Dale, 1999; Fischl, Sereno, Tootell, & Dale, 1999; Fischl, Van Der Kouwe, et al., 2004; Reuter et al., 2010; Ségonne et al., 2004). In addition, the segmentation precision was manually checked in all participants leading to the exclusion of one older adult because of failed surface reconstruction. Subsequently, cortical surface area (CSA) and cortical thickness (CT), the minimal distance between gray-white matter border and the pial surface at each vertex (Fischl and Dale, 2000), was extracted at each vertex of the tessellated surface. CSA is specified as the mean surface area of the pial surface area and the gray-white matter surface area of the region at the respective vertex. CT has been validated using manual segmentation (Cardinale et al., 2014; Kuperberg et al., 2003; Salat et al., 2004) and histological analysis (Rosas et al., 2002). Additionally, it has been shown to be reliable in healthy older adults (Liem et al., 2015). CT and CSA of six bilateral ROIs, which have been shown to be involved in auditory perception and speech processing (Giroud, Hirsiger, et al., 2018; Meyer et al., 2014) were extracted using the aparc.a 2009s annotation (Destrieux, Fischl, Dale, & Halgren, 2010): Planum Temporale (PT), Planum Polare (PP), Supratemporal Gyrus (STG), Supratemporal Sulcus (STS), Heschl's Gyrus (HG), Heschl's Sulcus (HS).

Statistical analyses

First, in order to statistically verify the occurrence of an MMN, we performed paired t-tests within each age group comparing the peak amplitude evoked by each of the two

deviants to the peak amplitude evoked by the standard. Thus, we compared the peak amplitudes of Deviant 1 and Deviant 2 to the Standard which were extracted time-locked to the three syllables of the word /Hubschrauber/, respectively. A comparison to a baseline, in this case to the signal evoked by the standard stimulus, is crucial because of the consistently lower EEG power measured on the scalp in older adults (see Figure 2.3). We expected to find MMNs evoked by both deviants when the EEG signal was time-locked to syllable 1, an MMN only evoked by Deviant 1 (but not Deviant 2) when the EEG was time-locked to syllable 2, and an MMN only evoked by Deviant 2 (but not Deviant 1) when the EEG was time-locked to syllable 3 (see hypotheses in Table 2.1). Importantly, we defined the occurrence of an MMN as a statistically significant difference (uncorrected for multiple comparisons) in the peak amplitude between deviant and standard. In order to stay consistent in our statistical analysis pipeline, we performed the same paired t-tests for the latencies. Furthermore, to also statistically investigate age-related differences in the MMNs, we used univariate ANOVAs correcting for PTA and gender and compared the MMN magnitude (the difference of the peak amplitude between deviant and standard) between the two age groups in all conditions in which a significant MMN occurred in both groups. Also, in order compare the MMN magnitude between the different conditions in which a significant MMN occurred, a repeated measure ANOVA correcting for PTA and gender was performed within each age group.

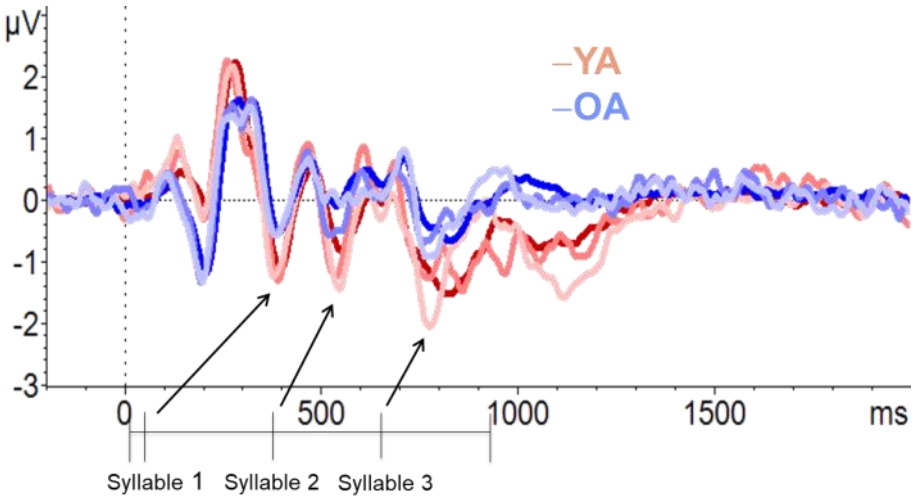

Figure 2.3. Figure 2.3 shows the ERP time-locked to word onset at electrode Cz, separately for each stimulus (dark = Standard, light = Deviant 1, very light = Deviant 2) and age group. Time-locked to the onset of each syllable, there are MMNs occuring after approximately 200 ms. Peak amplitudes were analyzed statistically time-locked to each syllable.

Second, the accuracy of the behavioral discrimination task was analyzed using a univariate ANOVA correcting for PTA and gender to compare age-related differences in discrimination of the stimulus material used for the MMN experiment, which only differed in the stress position within the word /Hubschrauber/ (stress either on the

first, second, or third syllable). In addition, we computed a repeated measure ANOVA correcting for PTA and gender using the factors syllable (Syllable 1, Syllable 2, Syllable 3), pitch difference (20 Hz, 30 Hz, 40 Hz), and age group (YA, OA) in order to assess discrimination performance difference with respect to age groups and pitch differences within syllables.

Third, age group differences between CT and CSA of the six bilateral ROIs were examined using univariate ANOVAs controlled for PTA and gender which were corrected for multiple comparisons by applying Bonferroni correction (alpha error divided by the number of tests) leading to a lowering of the alpha level from $\alpha = .05$ to $\alpha = .0042$ for the 12 ROIs compared between the two age groups (Giroud, Hirsiger, et al., 2018; P. C. Wong et al., 2010).

Fourth, in order to elucidate the relation between brain structure and brain function in the older adults, two-tailed partial correlations between MMN amplitudes and CT and CSA in the 12 ROIs were calculated using similar Bonferroni correction as explained above, while also correcting for PTA and gender. Furthermore, similar partial correlations were calculated with CT and CSA in the 12 ROIs and the behavioral data.

2.1.3 Results

Age-related differences in the mismatch negativity evoked by word stress

Unexpectedly, we did not find a MMN time-locked to Syllable 1 in the YA, neither for Deviant 1 nor for Deviant 2 (Deviant 1: t(14)=.93, p=.370, Deviant 2: t(14)=1.76, p=.101) (see Table 2.2 and Figure 2.4). However, in the OA, we found a MMN time-locked to Syllable 1 evoked only by the Deviant 1 (Deviant 1: t(22)=2.13, p=.045, Deviant 2: t(22)=.78, p=.443). Furthermore, as predicted, a MMN time-locked to Syllable 2 was evoked by the Deviant 1 only in both age groups (YA: Deviant 1: t(14)=2.33, p=.036, Deviant 2: t(14)=1.99, p=.066; OA: Deviant 1: t(22)=4.40, p<.001, Deviant 2: t(22)=1.66, p=.111). Also, in the OA we found a MMN time-locked to Syllable 3 evoked by the Deviant 2 only, as predicted (Deviant 1: t(22)=-.84, p=.408, Deviant 2: t(22)=2.44, p=.023). However, we did not find any MMN in the YA when time-locked to Syllable 3 (Deviant 1: t(14)=.31, p=.761, Deviant 2: t(14)=1.08, p=.298). The age group comparison between the MMN time-locked to Syllable 2 evoked by Deviant 1 (which was the only one we found in both age groups) did not yield a significant difference between YA and OA (F(1,34)=.73, p=.399). Also, the three significant MMNs which we found in the OA group, did not differ in magnitude from each other (F(2,40)=.85, p=.861). The same analyses for the latency revealed that there were no significant differences between deviants and standard stimuli (all t's<-1.66, all p's>.119), except for the signal time-locked to Syllable evoked by Deviant 2 in the OA (t(22)=2.30, p=.031).

Overall, these findings show that our data are not in accordance with Hypothesis 1.

Neither the YA, nor the OA evoked an MMN time-locked to Syllable 1 even though the deviants were slightly different from the standard stimulus in their pitch (18.05 Hz). However, we could find evidence for Hypothesis 2 in both age groups reveling that YA and OA process an unexpected word stress on Syllable 2 (with a difference of pitch to the standard stimulus of 73 Hz). Similarly, Hypothesis 3 was confirmed, and the analyses revealed that an unexpected word stress of 53.54 Hz on Syllable 3 was noted by the auditory circuits. However, only the OA were sensitive to this difference, not the YA.

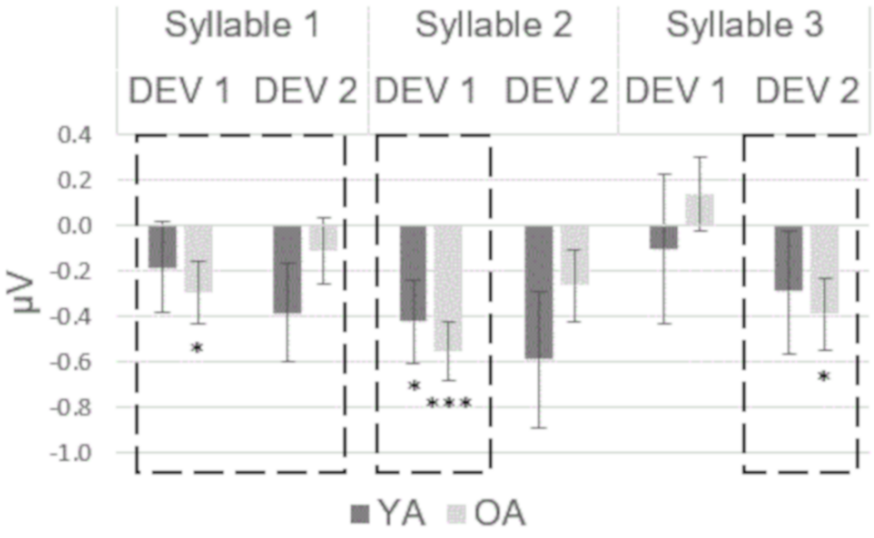

Figure 2.4. This Figure shows the peak amplitude differences between the deviants and the standard stimuli for each deviant condition separately for the time-locked signal to each of the three Syllable onsets. Dark grey indicates YA, light grey OA. *=p<.05 and ***=p<.001 indicating significant difference between deviant and standard peak amplitude implying a significant occurrence of an MMN. The dashed lined boxes point to the conditions in which we expected a significant MMN to occur.

Table 2.2

Table 2.2 shows the peak amplitudes and their respective latencies for each syllable and for each stimulus (Standard, Deviant 1, Deviant 2) and each age group (YA, OA) separately. Standard deviations are shown in brackets.

Peak amplitudes in μV

	Syllable 1		Syllable 2		Syllable 3	
	YA	OA	YA	OA	YA	OA
Standard	-1.14 (.75)	-.52 (.63)	-2.11 (1.13)	-1.50 (.75)	-.98 (.85)	-.90 (.60)
Deviant 1	-1.32 (1.06)	-.81 (.90)	-2.45 (1.41)	-2.06 (1.08)	-1.08 (1.22)	-.77 (1.09)
Deviant 2	-1.52 (1.23)	-.63 (.84)	-2.70 (1.71)	-1.77 (1.09)	-1.26 (1.02)	-1.29 (1.06)

Latencies of peak in ms

	Syllable 1		Syllable 2		Syllable 3	
	YA	OA	YA	OA	YA	OA
Standard	312.50 (37.77)	323.54 (12.06)	165.36 (22.88)	179.69 (52.18)	189.58 (46.90)	212.21 (33.87)
Deviant 1	319.01 (35.84)	325.32 (26.69)	172.27 (35.69)	187.16(54.35)	210.03 (59.91)	210.34 (41.92)
Deviant 2	334.64 (30.08)	330.84 (24.77)	179.69 (35.53)	196.76 (52.40)	196.88 (40.11)	191.07 (34.04)

Age-related differences in behavioral word stress perception

Both age groups performed high on the discrimination task using the same stimuli as in the MMN experiment (YA: 91.67 % correct, OA: 86.55% correct) and there was no statistically significant difference between the groups ($F(1,29)=.22$, $p=.64$). The repeated measure ANOVA with the factors syllable (Syllable 1, Syllable 2, Syllable 3), pitch difference (20 Hz, 30 Hz, 40 Hz), and age group (YA, OA) revealed a significant main effect of pitch difference ($F(2,58)=4.97$, $p=.01$, $\eta^2p=.15$) showing that the 20 Hz difference was the most difficult to perceive (49.10 % correct), while the 30 Hz difference was moderately difficult to perceive (68.13% correct), and the 40 Hz difference was the easiest to discriminate (78.62 % correct), all post hoc p's$<.025$ (see Figure 2.5). Furthermore, there was a main effect of age group ($F(1,29)=18.59$, $p<.011$, $\eta^2p=.39$) showing that the OA performed worse than the YA (YA: 83.56 % correct, OA: 47.01% correct) across all conditions. Furthermore, there was a significant interaction between syllable, pitch difference and PTA ($F(4,116)=2.55$, $p=.043$, $\eta^2p=.08$) suggesting that pitch differences were most difficult to discriminate on Syllable 1, moderate on Syllable 2 and easier on Syllable 3 and that this was particularly true for the 20 Hz difference.

Thus, these results suggest that the OA performed much worse across all conditions even though the PTA differences between YA and OA were controlled for and all participants did not have a hearing loss which would be diagnosed in the clinic. Furthermore, our results suggest that the 20 Hz word stress difference was too difficult to perceive for OA, especially on the first and second syllable. But also for the YA, the 20 Hz difference was the most difficult to discriminate, even though they performed better than

OA. Interestingly, across both age groups, this 20 Hz difference was also most difficult to discriminate when on the first syllable on which a word stress can be expected in the German language and on which the word stress is correct for the word /Hubschrauber/.

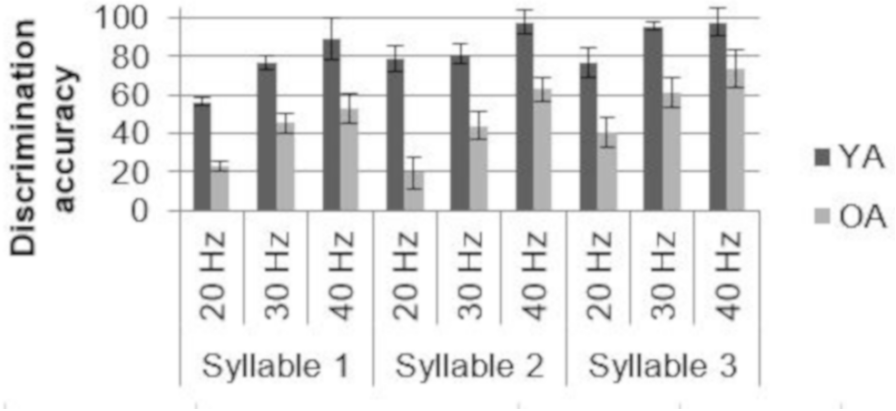

Figure 2.5. This Figure shows the accuracy for the word stress discrimination task when the word stress was different in 20, 30, or 40 Hz as well as when it was on the first, second, or third syllable of the word /Hubschrauber/. Dark grey indicates YA, light grey OA.

Age-related differences in auditory cortical structure

Similar to our previous study in which we published the cortical thickness data of a part of the participants included in this study (Giroud, Hirsiger, et al., 2018), the older adults had lower cortical thickness in all six left and right auditory brain areas than the younger adults (see Table 3), but similar cortical surface areas. This points to the fact, that the older adults in this sample experience age-related atrophy in bilateral auditory brain regions which is reflected in lower CT in these brain regions.

Table 2.3

This table shows the mean (M) and standard deviation (SD) of cortical thickness (CT) in mm and mean cortical surface area (CSA) in mm2 of all six bilateral ROIs for younger (YA) and older adults (OA) separately. Furthermore, F values for statistical comparison of CT and GMV between YA and OA are described.

CT

	YA		OA			
	M	SD	M	SD	F	p
l PT	2.65	.15	2.43	.12	F(1,34)=18.92	<.001 ***
l PP	3.58	.23	3.29	.29	F(1,34)=9.53	.004 *
l STG	3.08	.16	2.85	.16	F(1,34)=18.54	<.001 ***
l STS	2.52	.13	2.23	.11	F(1,34)=50.12	<.001 ***
l HS	2.62	.37	2.12	.35	F(1,34)=10.75	.002 *
l HG	2.59	.18	2.19	.22	F(1,34)=24.75	<.001 ***
r PT	2.61	.17	2.36	.16	F(1,34)=18.80	<.001 ***
r PP	3.63	.21	3.24	.30	F(1,34)=18.39	<.001 ***
r STG	3.19	.11	2.87	.17	F(1,34)=33.01	<.001 ***
r STS	2.55	.11	2.33	.14	F(1,34)=21.33	<.001 ***
r HS	2.87	.28	2.34	.25	F(1,34)=32.68	<.001 ***
r HG	2.62	.21	2.25	.24	F(1,34)=16.60	<.001 ***

CSA

	YA		OA			
	M	SD	M	SD	F	p
l PT	785.37	132.30	692.07	104.73	F(1,34)=11.71	.002 *
l PP	458.93	60.43	416.83	50.95	F(1,34)=7.38	.010
l STG	1852.20	170.33	1802.28	168.66	F(1,34)=.48	.490
l STS	3268.43	481.65	3185.61	427.26	F(1,34)=.35	.557
l HS	239.63	27.25	241.57	37.45	F(1,34)=.02	.903
l HG	434.90	90.93	371.85	54.75	F(1,34)=9.09	.005
r PT	550.23	82.77	518.04	62.10	F(1,34)=4.11	.050
r PP	457.30	63.03	433.37	58.65	F(1,34)=2.38	.132
r STG	1597.57	152.00	1557.07	161.25	F(1,34)=.55	.464
r STS	3975.37	392.90	3795.76	421.50	F(1,34)=2.23	.144
r HS	202.20	26.40	206.70	27.56	F(1,34)=.03	.869
r HG	310.80	49.90	273.50	40.64	F(1,34)=9.41	.004 *

Note: *p<.05 trend, *p<.0042, Bonferroni corrected, ***p<.001*.

The relation between brain structure and brain function

In order to investigate the structure-function relationship in the OA group, partial correlations between the extent of age-related auditory atrophy as measured by CT as well as CSA in the six bilateral auditory brain regions and the peak amplitude of the MMN were calculated. Because we did not find any significant differences between the magnitudes of the three MMNs which were significant in the OA, we created an average MMN in order to reduce the number of correlations we calculated. However, we did not find any significant correlations with the CT of the six bilateral regions, but with the CSA of the

left STG and the left HS (after correcting for multiple comparisons by applying a lowered α threshold of .0042 with r= -.62, p=.003 and r= -.65, p=.002, respectively). Thus, older individuals with higher mean surface area in these left auditory areas also evoked higher MMN amplitudes (see Figure 2.6).

Furthermore, we calculated similar partial correlations with brain structure and behavior in the OA group, specifically with the discrimination accuracy of the 20 Hz pitch differences, because this was the behavioral condition in which age-related differences were the strongest. We found one positive significant correlation (after correction for multiple comparisons), namely with the cortical thickness of the right STS (r=.69, p=.002). Thus, in this difficult perceptual task, older adults who had thicker right STS performed better.

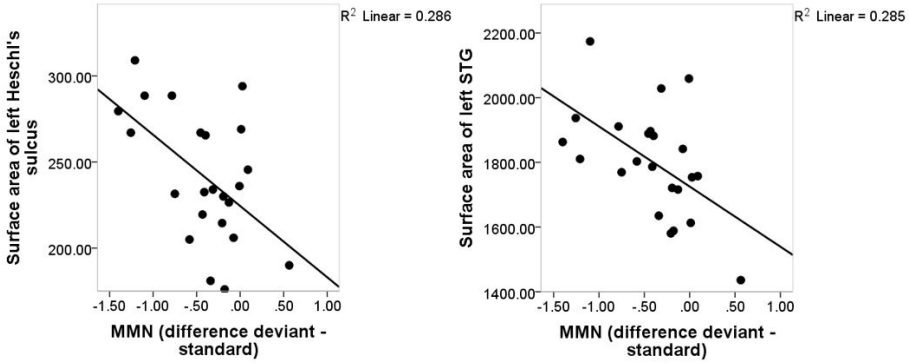

Figure 2.6. Figure 2.6 depicts the significant correlations between brain structure and MMN for the older adults. Older individuals who had larger surface area in the left Heschl's sulcus and in the left STG also evoked larger MMN magnitudes.

2.1.4 Discussion

The aim of the present study was to examine the relationship between central age-related hearing loss and prosody perception, particularly word stress perception, in younger and older adults with peripherally normal hearing. By means of the SBM approach, we were able to capture genetically determined (CSA) as well as experience-dependent (CT) neurostructural characteristics of auditory-related areas and its relations with neurofunctional (MMN) and behavioral parameters of word stress sensitivity. Furthermore, with our MMN paradigm we were able to disentangle bottom-up related as well as top-down controlled auditory perceptual processes in real-time during word stress perception time-locked to the different syllables in the same word. The results of the current study will be discussed in the following.

As predicted, we found that a pitch difference on the last syllable was easier to discriminate (for both groups) than on the second syllable. It has been shown that a stress on the last syllable is very uncommon in the German language (Jessen et al., 1995)

which may therefore capture the attention of listeners leading to a higher sensitivity to acoustic changes on the last syllable and therefore a better performance. However, the MMN do not reflect this behavioral result but rather reveal strong age-related differences as will be discussed in the following.

Our MMN results show that the older adults were more sensitive to varying pitch patterns in words than the younger adults, even though the two groups both discriminated the word stress variations of the word /Hubschrauber/ with a high accuracy in the behavioral task. This suggests that the older adult's MMN were more strongly driven by the acoustic differences in pitch and therefore by the acoustic properties of the stimulus material (i.e., bottom-up). Simultaneously, we assume that the younger adults did not evoke MMNs time-locked to syllables one and three because they relied more on their experience with the German language (i.e., top-down), in which word stress patterns do not mark linguistic properties relevant to understand a word. In other words, word stress patterns in the German language only rarely mark word meanings and are therefore not fundamental to understand the meaning of a word (Janßen, 2004). The younger adults still evoked an MMN time-locked to syllable 2, which had the most pronounced acoustic difference between the stressed and unstressed version with 73 Hz and therefore might have caught the attention of all participants regardless of its linguistic importance. A study which support these age specific patterns in bottom-up and top-down processing comes from the visual domain (Werkle-Bergner, Shing, Müller, Li, & Lindenberger, 2009). In this study, older adults showed more gamma phase-stability between trials evoked by small visual stimuli as compared to younger adults, suggesting higher temporal bottom-up stability in older adults which may be a result of compensatory effects because of higher neuronal loss (Werkle-Bergner et al., 2009). Such higher neuronal loss has also been shown to trigger compensatory effects in the auditory modality (Cabeza, 2002; Giroud, Hirsiger, et al., 2018). However, more research is needed to better understand the neural mechanisms behind the effect of age on the stability of bottom-up representations of auditory signals.

Interestingly, the generally lower performance of the older adults in the behavioral pitch discrimination task (discriminating 20, 30, and 40 Hz pitch differences on the same syllable) suggests that the higher word stress sensitivity in older compared to younger adults which we found in the MMN experiment does not result from a general higher sensitivity to pitch. Instead, we interpret this finding in such that older adults only show higher sensitivity to pitch when pitch is marking a syllable in a word (as measured by the MMN experiment) compared to when pitch indicates the strength of a syllable stress (as measured in the behavioral experiment). In that sense, syllable stress in a word has been shown to indicate the rhythm of a word, which may be an additional prosodic cue which older adults with difficulties to perceive the temporal fine structure of a word may use to improve speech perception.

For example, marked prosodic elements such as intonation and stress in speech, also called elderspeak, have been shown to be helpful for older adults to perceive speech and improve comprehension (Cohen and Faulkner, 1986). Similarly, older adults have been shown to be sensitive to prosodic speech cues to at least the same extent as younger adults (Wingfield et al., 2000, 1992). It is therefore possible that marked prosody such as in elderspeak may help older adults to compensate for age-related decline in temporal fine structure processing. Word stress as a prosodic cue indicating the word rhythm may therefore be more important for older adults than for younger adults during speech perception, explaining the higher sensitivity in the MMN experiment towards word stress violations. However, it has also been shown that not all types of prosodic marking are helpful for older adults, because slowing the speech rate and using high pitch has not been shown to improve understanding and can rather reflect aging stereotypes of the speaker (Kemper & Harden, 1999).

Still, this stronger focus on prosodic speech cues in older as compared to younger adults resembles some results from studies with babies. During the third trimester of gestation and therefore at a very early maturation stage structural brain asymmetries have even been observed to favor the right side in the superior frontal gyrus (SFG), the STG, and the HG (Dehaene-Lambertz, Hertz-Pannier, Dubois, & Dehaene, 2008). This right-ward lateralization in the auditory language network during neurodevelopment has been related to a stronger focus on suprasegmental speech cues such as prosody in babies, while during maturation and exposure to a specific language, the size of the left PT and the left HG is increasing to support the improved processing of temporal fine structure (Obrig, Rossi, Telkemeyer, & Wartenburger, 2010; Wartenburger et al., 2007). These findings are in line with the Asymmetric Sampling in Time (AST) framework (Poeppel, 2003) which has been confirmed by a number of studies (Abrams, Nicol, Zecker, & Kraus, 2008; Doelling et al., 2014; Giraud & Poeppel, 2012; Gross et al., 2013; Liem et al., 2014; Luo & Poeppel, 2007, 2012; Peelle & Davis, 2012; Rufener, Oechslin, Wöstmann, Dellwo, & Meyer, 2016) in that they fit the AST predictions that left and right auditory cortices preferentially entrain to sounds at different rates; the left auditory areas prefer to process rapidly changing acoustic information at approximately 40 Hz (gamma band) such as temporal fine structure, whereas the right auditory areas preferentially process slower acoustic cues at approximately 4 Hz (theta band) such as prosodic cues. Thus, similar to babies who still have to learn the temporal fine structure of the specific language of their environment, older adults who have central age-related hearing loss and show difficulties with the processing of temporal fine structure focus more strongly on suprasegmental elements of speech.

Furthermore, similar to babies, it has been shown that the structure (i.e., cortical thickness) of right auditory areas is relevant for auditory perceptual performance in older adults (Giroud, Hirsiger, et al., 2018). In other words, less age-related atrophy in right

auditory areas such as the PT and the HS – and therefore less central hearing loss – has been shown to be related to better performance in supra-threshold frequency selectivity, supra-threshold temporal compression, as well as speech-in-noise perception in older adults (Giroud, Hirsiger, et al., 2018). Similarly, higher white-matter integrity in the right superior longitudinal fasciculus and the right uncinate fasciculus was associated with better hearing performance in older adults (Rigters et al., 2018). Furthermore, older adults have been shown to have stronger right-lateralization of auditory theta oscillations in resting state EEG (Giroud, Hirsiger, et al., 2018) reflecting an intrinsic imprint of stronger right auditory preference to process slowly changing auditory cues such as prosody which have been shown to entrain to the theta band during active processing (Giraud et al., 2007; Giraud & Poeppel, 2012; Morillon et al., 2012; Poeppel, 2003). In sum, there is growing evidence that prosodic cues play a strong role in speech perception in older adults and, similar to younger adults (Hurschler et al., 2013; Liem et al., 2014; Meyer et al., 2002; Meyer, Steinhauer, Alter, Friederici, & von Cramon, 2004), right auditory areas seem to preferentially support that function.

In the current study, we also assessed cortical thickness to capture age-related central hearing loss in left and right auditory areas. Similar to our previous study (Giroud, Hirsiger, et al., 2018), we found a significant correlation revealing that older adults who had less age-related atrophy (i.e., thicker) right STS performed better in the 20 Hz pitch discrimination task (R2=.48). Thus, cortical atrophy explained 48% more variance than pure-tone thresholds in the pitch discrimination task, highlighting the importance of considering central hearing loss when investigating speech perception in older adulthood. Since audiograms are not able to capture such age-related differences in auditory perception, we believe it is crucial to include such alternative measures to assess hearing loss in older adults.

However, we did not find any relation with cortical thickness in auditory areas and the MMN evoked by word stress, but then there was also no age-related decline in word stress perception as indicated by the MMN results. Still, our analyses revealed a significant correlation between cortical surface area in the left STG and the left HS and the MMN in older adults. We interpret this finding as first evidence that older adults who have genetically determined larger cortical surface area (Pontious et al., 2008) in left auditory brain regions, may to some degree be protected against auditory decline in that they may better be able to use sensory-driven prosodic cues in a speech signal. As argued by Meyer et al. (2014), larger CSA in left auditory-related areas reflect more widely spaced neuronal columns which enables to recognize and store over-learned spectro-temporal acoustic patterns in a efficient and automatic manner. Thus, it is likely that larger CSA in left auditory regions allows older adults to perceive complex spectro-temporal patterns until old age.

2.1.5 Conclusions

Our results suggest that older adults are more sensitive to bottom-up driven word stress patterns than younger adults even though they show poorer performance in pitch discrimination, which is related to age-related structural decline (i.e. lower cortical thickness) in right auditory areas. Thus, we found a relationship between central hearing loss and suprasegmental speech perception in older adults. Furthermore, larger cortical surface area in left auditory areas was associated with larger MMN amplitudes evoked by word stress violations. Thus, prosodic speech cues such as word stress may be helpful for older adults who experience central age-related hearing loss, while genetically determined larger CSA in left auditory areas may be protective against central age-related hearing loss in that it is involved in allowing to perceive prosodic speech cues with high accuracy.

2.1.6 Acknowledgments

This research was supported by the Swiss National Science Foundation (grant nr. 105314_152905 to MM). We thank Allison Christen for invaluable proofreading of the manuscript.

2.2 Article II: Neuroanatomical characteristics of speech in noise perception in older adults with mild hearing loss.

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A similar version of this manuscript is currently in preparation for submission

Abstract Difficulties in understanding speech in noisy environments is a major complaint of older adults. To gain further insights into the relationship between speech-in-noise (SiN) perception, age-related neurostructural plasticity and cognition, twenty-five older adults with mild presbycusis and thirteen younger adults were investigated. Cortical thickness (CT) and cortical surface area (CSA) were determined from each participants T1-weighted MR image. In addition, older participants' working memory capacity, inhibtion and vocabulary were measured. CT and CSA were correlated with performance scores of SiN to identify anatomical regions important for SiN perception. While several peri-sylvian and frontal regions showed a significant negativ relationship with SiN for CT (i.e. individuals with higher CT performed better in the SiN task), no relationships were found for CSA. CT, extracted from regions significantly correlated with SiN, and age were then entered as predictors into a multiple regression analysis with SiN performance as a dependent measure. CT in a right inferior frontal region emerged as a significant predictor of SiN perception. In addition, age modulated the relation between CT in a superior frontal cluster and SiN, where a thicker cortex was associated with better auditory performance only in older adults. The relationship between superior frontal gyrus and SiN exclusive to older adults suggested a relationship with cognitive abilities, in particular working memory. A multiple regression with CT of left superior frontal gyrus as dependent variable and working memory capacity as predictors indicated that SiN and the interaction between SiN and working memory significantly predicted CT. The interaction suggested that in individuals with higher working memory capacity the relationship between SiN performance and CT was strongest. In summary, these results suggest that CT in superior frontal regions was associated with SiN performance in older adults in particular and that this relationship within the old group was modulated by working memory capacity. The results are discussed in light of previous work on SiN perception and neuroanatomy in aging and offers potential explanation for diverging reported therein. In general, the results presented here provide further insight into the relationship between SiN perception and brain structure in older adulthood.

2.2.1 Introduction

The prevalence of age-related hearing loss (presbycusis) increases with increasing age (Brant & Fozard, 1990; Cruickshanks et al., 1998; Roth et al., 2011; Wiley et al., 2008) and presbycusis is the third most chronic condition in adults aged above 65 years (Yueh et al., 2003). Age-related presbycusis has been described as a disorder that encompasses reduced hearing sensitivity, impairments in temporal processing and in the localization of sound sources, as well as difficulties understanding speech in noisy environments (Gates & Mills, 2005). Different types of pathologies related to age-related presbycusis have been described by Schuknecht (1964), including sensory, neural, metabolic and mechanical age-related presbycusis. Hereby, sensory refers to atrophy of the organ of corti (i.e. the loss of inner ear hair cells) and the auditory nerve, neural refers to a loss of neurons in the auditory pathway and the cochlea, metabolic refers to deterioration of the stria vascularis and mechanical refers to a stiffening of the basilar membrane.

In practice, presbycusis has been mainly understood as peripheral sensory presbycusis that is measured by pure-tone audiometry (Humes et al., 2012). Pure-tone thresholds mainly reflect audibility of auditory signals, but do not seem to be a good descriptor for speech intelligibility per se (Giroud, Hirsiger, et al., 2018). For example, a major real-life complaint of elderly is that they have difficulties understanding speech in presence of background noise (Anderson et al., 2011), which is reflected lower tolerance to background noise for the comprehension of spoken language in older adults (Giroud, Hirsiger, et al., 2018; Helfer & Wilber, 1990). It has been demonstrated that speech-in-noise (SiN) perception difficulties can only partly be explained by elevated pure-tone thresholds (Cruickshanks et al., 1998; Dubno et al., 1984; Gordon-Salant & Fitzgibbons, 1993; Killion & Niquette, 2000; Souza et al., 2007). Hence, it seems to be the case, that there have to be factors apart from peripheral presbycusis that account for variance in SiN perception.

On top of difficulties in SiN perception, previous research indicated lower performance in older compared to younger adults in time compressed spoken language perception (Gordon-Salant & Fitzgibbons, 1993), temporal order discrimination tasks (Fogerty et al., 2010, 2012), fricative discrimination tasks (Giroud, Lemke, et al., 2018) and in gap detection tasks (Harris et al., 2010). In summary, these results imply that other factors than peripheral presbycusis contribute to speech perception difficulties particular to older adults. The idea, that an age-related decline in the neural processing of speech in the auditory brainstem and in cortical auditory regions may contribute to an age-related decline in SiN perception, has gained traction in recent years (Humes et al., 2012). According to Humes et al. (2012) hearing difficulties in older adulthood arise from an interplay between central and peripheral presbycusis in combination with cognitive factors. This means that work investigating speech comprehension in older adulthood

should consider peripheral hearing as well as central factors and cognition.

However, the definition of central presbycusis is, rather broadly, defined as age-related atrophy of cortical and subcortical regions (Humes et al., 2012). Evidence from neuroimaging studies demonstrates that older adults show atrophy in various brain regions compared to younger adults Fjell and Walhovd (2010); Fjell et al. (2009, 2012); Giroud, Hirsiger, et al. (2018); Hogstrom et al. (2012); Raz et al. (1997); Sowell et al. (2003). Neuroanatomical alterations as a function of peripheral presbycusis have also been described (Eckert et al., 2012; Husain et al., 2011; Peelle et al., 2011; Profant et al., 2014). In those studies, a link between presbycusis and decrease of cortical gray matter volume (CV) has been shown. This suggests that presbycusis is related to morphometric differences in the brain, however it might be that the driving factor is age and not peripheral presbycusis per se (Giroud, Hirsiger, et al., 2018; Profant et al., 2014). Indeed, work, including older adults with no impairments in peripheral hearing, has shown that there are still differences between older and younger adults in brain morphology related to auditory processing that cannot be explained by peripheral hearing-loss (Giroud, Hirsiger, et al., 2018). Along this line it has been stated that SiN perception correlates more strongly with age than with hearing-loss (Vermeire et al., 2016).

Accordingly, anatomical measures in several brain regions have been implicated to be specifically involved in SiN perception in older adulthood and thus to be sensitive to plastic processes. Cortical thickness (CT) in primary auditory and inferior and superior frontal areas have been reported to be a predictor for SiN performance in older adults, whereas a thicker cortex was related to better performance (Giroud, Hirsiger, et al., 2018; P. C. Wong et al., 2010). Therefore, these results suggest that CT is sensitive to plastic processes across the lifespan and can explain some of the variance in SiN perception. Further, CT is assumed to be a measure sensitive to lifespan neuroplastic alterations while CSA is assumed to be relatively stable (Bermudez et al., 2008; Engvig et al., 2010; Giroud, Hirsiger, et al., 2018; Meyer et al., 2014; Rakic, 1988, 1995, 2007).

However, the results from those two studies investigating the relationship between neuroanatomy and SiN perception in an aging context, are not entirely congruent in terms of which anatomical locations were reported to be related to SiN perception. P. C. Wong et al. (2010) report that CT of left superior frontal gyrus was correlated with age across a group of younger and older adults and that only within the older group was a significant predictor of SiN performance. Giroud, Hirsiger, et al. (2018) also investigated older and younger individuals and report that CT in the pars orbitalis and pars triangularis of the left inferior frontal gyrus were significant predictors of SiN performance. In addition two interactions with age suggested that only in older adults right Heschl's sulcus and right pars orbitalis were predictors of SiN performance. While Heschl's sulcus and and inferior frontal gyri are generally considered to be part of the language network(e.g. Friederici & Alter, 2004; Hickok & Poeppel, 2004), dorsal pre-

frontal regions are usually considered to be involved in executive functions (e.g. Elliott, 2003). In an fMRI study of SiN perception (P. C. Wong et al., 2009) it was reported that in comparison to younger adults activation in the auditory cortex was reduced in older adults while activation in prefrontal and precuneus areas– which, according to the authors, represent working memory and attention related regions–was increased. The authors interpretation was that non-auditory regions were recruited in a top-down compensatory way in the older adults. Hence, P. C. Wong et al. (2010) hypothesized that cognition and cortical regions related to cognition are integral for SiN perception, while Giroud, Hirsiger, et al. (2018) highlighted the importance of the integrity of auditory areas for successfull auditory performance in older adulthood. Thus, a potential explanation for the differences between P. C. Wong et al. (2010) and Giroud, Hirsiger, et al. (2018) could be that one group relied more strongly on cognitive strategies, while the other one dependent more on bottom-up processing.

A potential relationship between SiN perception and cognitive factors has been suggested in previous work, for example for lexical-access (Kaandorp et al., 2016), working memory (Gordon-Salant & Fitzgibbons, 1997) or inhibition (K. L. Tremblay et al., 2002). The importance of cognitive processes for language understanding is stressed in the ease of language understanding (ELU) model (Rönnberg, 2003; Rönnberg et al., 2013, 2008). This model proposes that, in the case where sensory input doesn't match lexical representations in the long term memory, working memory based restoration processes come into play. In this restoration process semantical and phonological information in the long term memory is assessed in an attempt to fill the gaps in the sensory input. This implies, that in particular for individuals with decline in sensory functioning, cognition is an important factor of language understanding.

The overall aims of this study were a) to gain further insight into the relationship between central presbycusis and SiN perception and b) to shed light on to potential reasons for differences in results in previous studies. A group of normal-hearing younger and a group of older adults with mild presbycusis were investigated. Participants underwent structural MR imaging and SiN perception testing. In addition, cognitive abilities of the older participants were evaluated. Cognitive testing included the assessment of working memory capacity (auditory *n*-back), inhibition (stroop test) and vocabulary (Mehrfachwahl-Wortschatz-Intelligenztest). These abilities were chosen based on previous work reporting relationships between SiN perception and cognition (Gordon-Salant & Fitzgibbons, 1997; Kaandorp et al., 2016; K. L. Tremblay et al., 2002).

In a first step, aimed replicating the results of Giroud, Hirsiger, et al. (2018) and P. C. Wong et al. (2010) in terms of the brain regions related to SiN perception in older adulthood, anatomical MRI images from younger and older adults were obtained and correlations between anatomical measures (i.e. CT and CSA) and SiN perception performance were calculated. Following this, regions that showed a significant relationship

with SiN scores across groups as well as age were entered as predictors into multiple regression analysis with SiN as dependent variable to determine for which clusters the relationship was modulated by age. To examine how interindividual differences in cognition moderate the relation between brain structure and SiN perception in older adults with mild presbycusis, anatomical measures of regions that were related to SiN only within the group of older participants were entered as dependent variables in a regression model with cognitive abilities as predictors.

We expected that older adults speech comprehension would be more vulnerable to background noise as compared to younger adults (Giroud, Hirsiger, et al., 2018; Helfer & Wilber, 1990) and that hearing thresholds would not predict SiN perception (Cruickshanks et al., 1998; Dubno et al., 1984; Gordon-Salant & Fitzgibbons, 1993; Killion & Niquette, 2000; Souza et al., 2007). In general we expected to find anatomical measures of the peri-sylvian, inferior and superior frontal regions to be related to performance in a SiN task across age-groups(Giroud, Hirsiger, et al., 2018; P. C. Wong et al., 2010). Because of the hypothesized importance of cognition for language understanding in particular in the presence of sensory decline (Rönnberg, 2003; Rönnberg et al., 2013, 2008) and since mild presbycusis was present the older individuals under investigation here, we expected areas related to cognition to be related to SiN perception particularly in the old group. Within these regions we hypothesized that cognitive abilities are related to anatomical measures (P. C. Wong et al., 2010). In addition, we expected cortical thickness to be a measure reflecting neuroplastic alterations along the lifespan (Giroud, Hirsiger, et al., 2018; Rakic, 1988, 1995, 2007), while CSA was expected to be more robust against age-related decline. Thus we expected that relationships between SiN perception and anatomical measures would be mainly found for cortical thickness, but less so for cortical surface area. In the same way we also expected that age group differences in relevant areas mainly exist for cortical thickness.

2.2.2 Materials and methods

Participants

Twenty-Seven older adults (OA) were initially included in the study. After data collection two participants were excluded from the analysis presented here because their speech-in-noise scores were above two standard deviations away from the group mean, which was considered to be atypical. This resulted in Twenty-Five OA (age range = 65-80 years, M_{age}=70.88, 12 females) and Thirteen and younger adults (YA)(age range = 20-29 years, M_{age}=24.15, 10 females) who participated in this study. Older participants were screened for cognitive impairment upon entering the study and all individuals scored at least 27 points in the Mini-Mental State Examination (MMSE) (Folstein et al., 1975). Out of these nobody reported any history of psychological or psychiatric disorders or

brain injuries. None of the participants was using hearing aids and they all reported to have no speech or hearing impairments. Both, YA and OA, were native (Swiss-) German speakers and did not learn any second language before the age of seven years. The Annett Hand Preference Questionnaire (Annett, 1970) indicated that all participants were right-handed. Other data acquired from the groups investigated here have been reported in prior publications (younger adults: Giroud, Hirsiger, et al. (2018), older adults: (Keller, Neuschwander, & Meyer, n.d., currently under review)) . Participants were paid for their participation and gave informed written consent. Data collection has been approved by the ethics committee of the Canton of Zurich.

Audiometry

Audiometric testing was performed in a double-walled, sound-attenuated booth at the University Hospital of Zurich.

Peripheral hearing: absolute thresholds

Pure tone thresholds were measured for 500, 1000, 2000 and 4000 Hz using a probe-detection paradigm were pure tones were presented for 250 ms (Lecluyse & Meddis, 2009; Lecluyse et al., 2013). Tones were delivered via custom-written Matlab software to circumaural headphones (Sennheiser HD 280-13 300 Ω). Participants responses were recorded with a touch screen (ELO AccuTouch, version 5.5.3.6.) while seated in front of it. Only participants with hearing thresholds below 40 dB were included in this study. While the younger group did not show any impairment, the older group displayed elevated thresholds that correspond to a mild impairment in hearing, according to the World Health Organization (WHO)(see Figure 2.7).

Central hearing: speech-in-noise sentence intelligibility

Speech-in-noise (SiN) performance was assessed with the OLSA Matrix Sentence Test (Wagener et al., 1999a, 1999b, 1999c). In this test, 50% SiN reception thresholds is measured with an adaptive approach. Sentences and noise were presented simultaneaously to the participants and after each sentence they were asked to repeat as many words as possible from the preceeding sentence. Sentences were low-context sentences to prevent participants from guessing the correct answer due to the sentences' context and the noise was generated by 30 overlays of the whole test material, which led to low amplitude modulation noise in the same spectrum as the test sentences. At the beginning of the testing procedure sentences and noise were presented at 65 dB SPL. After that sentence level was varied until the participant was able to correctly repeat 50% of the words of the sentence. Participants were seated in front of the speaker which

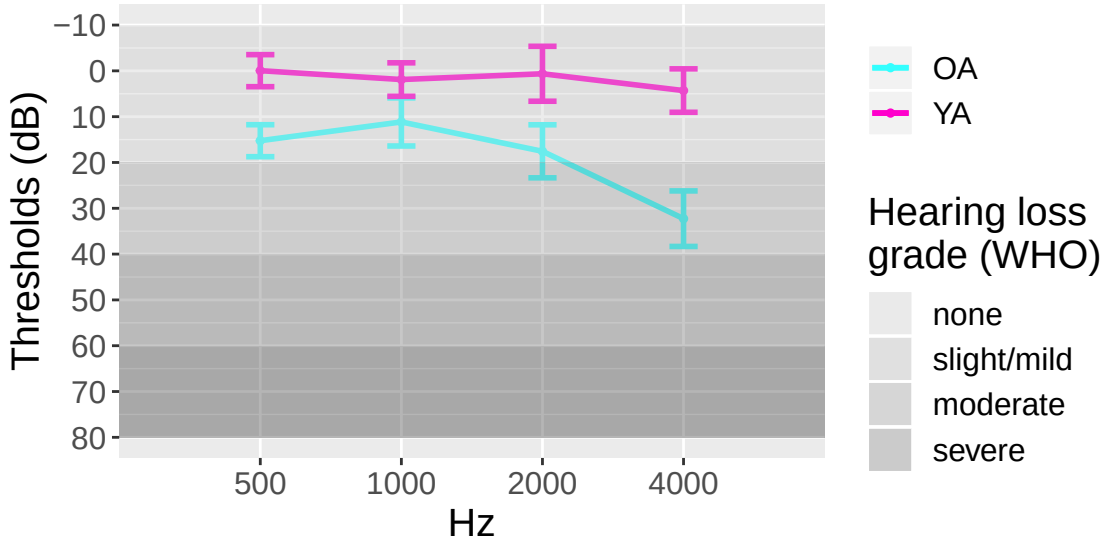


Figure 2.7. Pure tone hearing threshold averages of the older group. The World Health Organization (WHO) classification of hearning loss is displayed on the right. Error bars indicate 95% confidence intervals.

were positioned 0° azimuth and 1.5 m away from the subject's head. Sentences were presented via MACarena software.

Cognitive testing

The older group was assessed for different cognitive abilities to explore potentail relationships between brain anatomy, SiN performance and cognition.

Vocabulary

Mehrfachwahl-Wortschatz-Intelligenztest (Lehrl, 1999) was used as a proxy for the ability of individuals to use contextual information. Hereby, participants are presented with lists of four words. Out of those four words only one is an existing word (e.g. koze - tose - *nose* - nuse). Participants are asked to identify the existing word for every list of words. Correct answers are then summed up and transferred to IQ scores, giving an indication of participants vocabulary size. Wordlists were given on a sheet of paper and participants were asked to cross out the correct word.

Working memory

Working memory performance was assessed with an auditory *n*-back paradigm (Nystrom et al., 2000; Owen, McMillan, Laird, & Bullmore, 2005). Letter sounds were played to the participants from a computer and they were asked to identify whether the letter was the same as the one from n steps earlier. Each participant completed a 2-back and a

3-back run each consisting of 50 letters including 19 matches in total. Inter-stimulus-interval between letters was four seconds and participants indicated a match to the letter presented n steps back by pressing the space bar. Participants performance was defined as the ration between total responses given and correct responses for both runs.

Inhibition

A version of the stroop test (Stroop, 1935) was used as a measure of inhibition. Words reffering to colors were presented to the participants on the screen of a computer. The words were displayed in different colors either congruent to the word meaning (e.g. the word 'blue' displayed in blue color) or incongruent to it (e.g. the word 'blue' displayed in yellow color). Particpants were asked to indicate which color the word was displayed in by pressing a colored button on a keyboard. Interference scores were calculated as the difference between reaction times in congruent and incongruent trials.

MR acquisition and image processing

Structural images were recorded using a T1 weighted turbo field echo sequence (160 saggital slices, in-plane resolution = 0.94 x 0.94, slice thickness = 1 mm, matrix size = 256 x 256 mm, FOV = 240 X 240 mm, repetition time [TR] = 8.15 ms, TE = 3.74 ms, flip angle = 90°). T1 images were analyzed with FreeSurfer image analysis suite (version 6.0.0., `http://freesurfer.net/`). Using the surface-based morphometry (SBM) approach implemented therein, cortical surface models of all participants were obtained automatically (Dale et al., 1999; Fischl et al., 2001, 2002; Fischl, Salat, et al., 2004; Fischl, Sereno, & Dale, 1999; Fischl, Sereno, Tootell, & Dale, 1999; Ségonne et al., 2004). After segmentation, surface reconstructions were checked for accuracy. For one subject white matter segmentation errors were found, which were then corrected manually. The resulting surface models yield measures of cortical thickness (CT) and cortical surface area (CSA). Hereby, CT denotes the shortest distance between the gray/white matter border and pial surfaces and CSA the mean area of the triangular region at the respective vertex. Each participant's reconstructed brain was morphed to an average surface and smoothed using a FWHM kernel of 10 mm (Meyer et al., 2016). These were then entered to the built-in general linear model (GLM) facility of FreeSurfer for statistical analyses.

Statistical analyses

Statistical analyses were performed using R software (R Core Team, 2017). To test for differences between age groups in SiN performance an independent sample t test was calculated. Mean hearing thresholds, participants'age and their interaction were entered as predictors in a multiple regression model with SiN score as dependent variable to test

if age and hearing loss were related to listening to spoken language in noise. To identify regions where CT or CSA was related to SiN performance, SiN score was entered as a regressor in the FreeSurfer GLM facility with the respective anatomical measure as dependent variable. The resulting models were corrected for multiple comparison by applying Monte Carlo Null-Z simulation with an vertex-wise/cluster-forming threshold of $p<.001$ and a cluster threshold of $p<.05$ for each hemisphere independently. Anatomical measures of the significant clusters were then extracted and submitted to further analysis. Independent samples t tests were performed to compare CT and CSA between the two age groups for each anatomical region. In this case P-values were Bonferroni corrected for the number of regions compared within each anatomical measure. To assess whether age modulates the relationship between anatomy and SiN performance, multiple linear regression models including gender, z-standardized measures of PTA, anatomy and the interaction between age group and each anatomical measure as predictors and SiN performance as dependent variable were calculated. Relationships between SiN performance, anatomy and cognition were evaluated by entering z-standardized cognitive measures and their individual interaction with SiN performance as predictors in a multiple regression model with the anatomical measure of the region in question as dependent variable.

2.2.3 Results

SiN performance, age and hearing

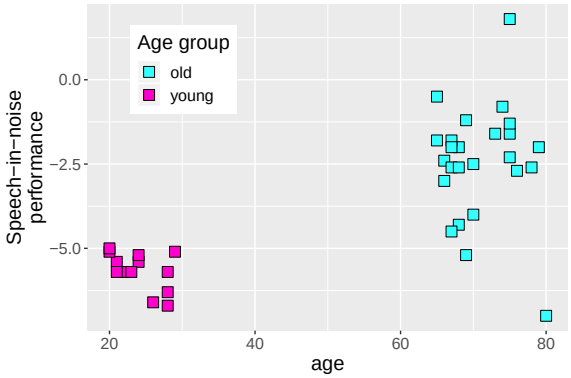


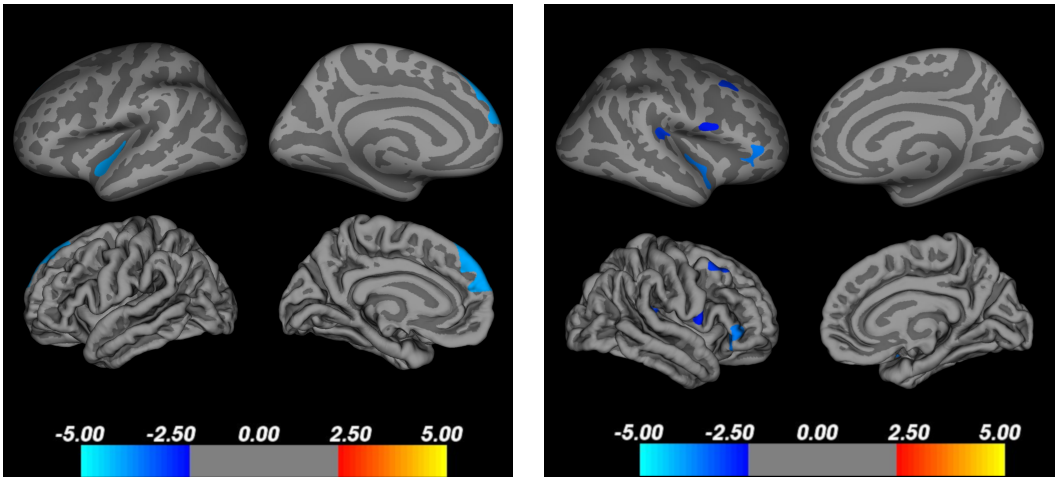
Figure 2.8. Performance scores of the speech-in-noise test.

Independent sample t test revealed that there was a significant difference in SiN performance ((t(32.32) = 8.68, p = <.001, M_{old} = -2.42, M_{young} = -5.66). Lower values indicate more tolerance against background noise, i.e. a better performance in the SiN task. OAs' tolerance against background noise thus was significantly worse than YA (see figure 2.8). A regression model including age, hearing threshold and their interaction was significant (F(3,34)=13.33, $p<.001$, adjusted R^2=0.5). Age was the

only significant predictor of SiN (β=0.85, p=.039).

Whole-brain analysis results

The FreeSurfer GLM analysis revealed several clusters in both hemispheres that were significantly correlated with SiN for CTs across both groups (Figure 2.9). The cluster statistics are presented in table 2.4 with the annotations drawn from FreeSurfer. Significant relationships between CT and SiN were found in superior temporal regions bilaterally, right hemisphere inferior frontal, caudal middle frontal and precentral regions and in a left hemispheric superior frontal region. CT in all clusters was negatively correlated with SiN indicating that individuals with thicker cortices in these regions performed better in the SiN task.



(a) View of the LH. *(b)* View of the RH.

Figure 2.9. Results of the whole-brain FreeSurfer analysis including both age groups. Results are displayed on the inflated and the pial surface.

The analysis for CSA did not reveal any significant clusters after correcting for multiple comparisons.

Table 2.4

Statistics of the negative correlations between cortical thickness and speech-in-noise performance in both hemispheres.

				Talaraich coordinates		
Annotation	Max	NVtxs	Size (mm^2)	X	Y	Z
LH						
superiorfrontal	-5.079	1234	676.34	-7.6	56.8	17.7
superiortemporal	-5.804	930	428.28	-44.5	-9.5	-13.0
RH						
superiortemporal	-4.468	722	302.81	41.9	-12.8	-10.3
parstriangularis	-5.449	488	295.78	48.4	34.2	-1.8
superiortemporal	-4.911	616	259.52	42.3	-34.0	14.2
caudalmiddlefrontal	-4.522	380	251.51	35.2	18.9	44.1
precentral	-6.614	474	223.33	56.5	5.8	11.5

Note:
LH: Left hemisphere, RH: Right hemisphere
Max: log10(p) at peak vertex (values $<$ -3 correspond to $p < 0.001$)
NVts: number of vertices above threshold ($p < 0.001$, cluster-corrected).

Group differences in cortical surface area and cortical thickness

Independent samples *t* tests revealed that CT was different between age groups in all regions (table 2.5). Consistently, YA cortices were thicker than those of the OA. For CSA no significant differences between age groups were found after correcting for multiple comparisons (table 2.6). Thus, significant age group differences were found for CT but not for CSA (figure 2.10).

Table 2.5

Group differences old-young: CT (P-values are bonferroni corrected).

	Old Adults		Young Adults			
Annotation	M	SD	M	SD	t	p
LH						
superiorfrontal	2.754	0.25	3.062	0.2	t(36)=-3.885	.003**
superiortemporal	2.309	0.23	2.655	0.19	t(36)=-4.624	<.001***
RH						
superiortemporal	2.493	0.24	2.852	0.22	t(36)=-4.43	.001**
parstriangularis	2.471	0.22	2.727	0.16	t(36)=-3.615	.006**
transversetemporal	2.122	0.21	2.451	0.19	t(36)=-4.772	<.001***
caudalmiddlefrontal	2.608	0.24	2.882	0.27	t(36)=-3.168	.022*
precentral	2.51	0.23	2.951	0.2	t(36)=-5.917	<.001***

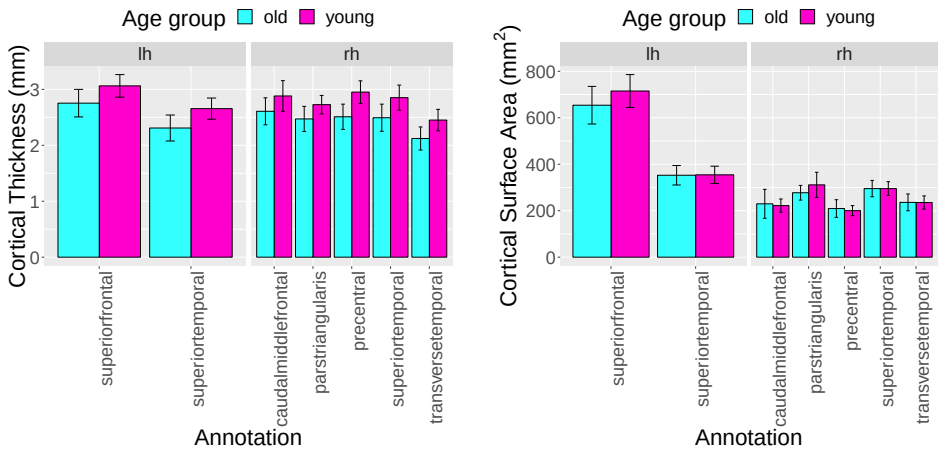
Note:
*$p < .05$, **$p < .01$, ***$p < .001$

Table 2.6

Group differences old-young: CSA (P-values are bonferroni corrected)

	Old Adults		Young Adults			
Annotation	M	SD	M	SD	t	p
LH						
superiorfrontal	654	0.24	715.077	0.22	t(36)=-2.298	.192
superiortemporal	352.56	0.22	354.385	0.16	t(36)=-0.132	1
RH						
superiortemporal	295.12	0.21	295.077	0.19	t(36)=0.004	1
parstriangularis	277.24	0.24	311.231	0.27	t(36)=-2.45	.135
transversetemporal	235.84	0.23	235.308	0.2	t(36)=0.046	1
caudalmiddlefrontal	229.64	0.51	221.923	0.44	t(36)=0.422	1
precentral	209.32	4.65	200.308	3.31	t(36)=0.788	1

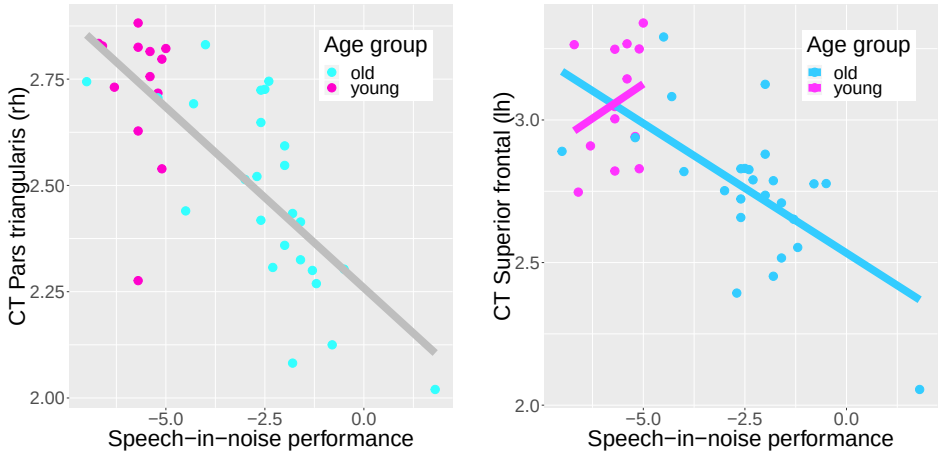
Note:
*$p < .05$, **$p < .01$, ***$p < .001$



(a) Cortical thickness *(b)* Cortical surface area

Figure 2.10. Age group differences in CT (a) and CSA (b). Younger adults displayed thicker cortex in all regions (all p's $<$ .05, bonferroni corrected), while no age group differences were found for CSA (all p's $>$ .05, bonferroni corrected).

Multiple regressions



(a) Relationship between CT and SiN in right pars triangularis region.

(b) Interaction with age group for CT in left superior frontal region.

Figure 2.11. Significant relationships between CT in the regions and speech in noise performance.

In order to test whether the relationship between CT, CSA and SiN was modulated by age, CT and CSA of all regions and their interactions with age group were entered in a multiple regression with speech-in-noise performance as dependent variable. Additionally, mean PTAs were entered in the regression model to control for individual differences in hearing sensititvity. The results from the regression with CT ($F(17,20=16.98$, $p<.001$, adjusted $R^2=0.88$) indicated that a thicker cortex in the pars triangularis cluster in the RH significantly predicted speech in noise performance (β=-0.45, p=.004) in both groups (figure 2.11a). An additional interaction suggested that only in older adults, a thicker

superior frontal cortex predicted better speech in noise (β=0.24, p=.041)(figure 2.11b). It can be assumed that this relationship was not due to individual differences in PTA within the older group since it was controlled for hearing thresholds. Thus, the question is whether a thicker cortex in left superior frontal gyrus is related to better cognitive abilities and whether this is ultimately the underlying reason for better performance in the SiN perception task. For the multiple regression with CSA (F(18,19=2.99, p=.011, adjusted R^2=0.49) age group was the only significant predictor (β=-1.11, p=.002).

Relation between SiN, Cognition and superior frontal region in older adults

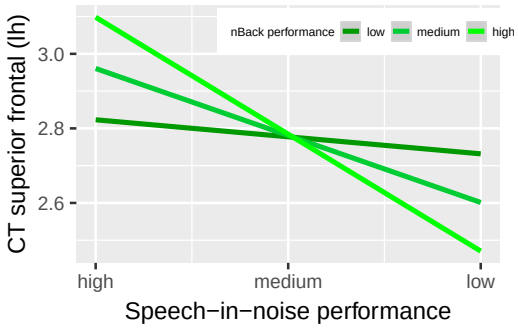


Figure 2.12. Interaction between speech-in-noise performance and working memory.The relationship between speech-in-noise performance and cortical thickness in the left superior frontal region is stronger for individuals with better working memory.

The only region that was related to SiN performance exclusively in the older group was the superior frontal gyrus. The importance of this region for the older group suggested that cognitive abilities were important within the older group to understand speech in background noise. Further, the same region was reported by P. C. Wong et al. (2010) and they hypothesized that the relationship of this region with SiN perception was reflecting the importance of working memory for listening to speech in background noise. This represents a strong a priori hypothesis in terms of the relationship between cognition, brain anatomy and speech in noise perception. Thus, working memory capacity together with SiN scores and their interaction were entered in a multiple regression model with CT of left superior frontal region as dependent variable. In a second step the remaining cognitive variables and their interaction with SiN were entered into the model. Finally, the first and the second model were compared to see whether the model including all cognitive variables could explain significantly more variance. SiN performance (β=-0.72, p=<.001) and the interaction between speech-in-noise and n-back (β=-0.41, p=.013) significantly predicted cortical thickness in the left superior frontal gyrus region (F(3,20=8.66, p.001, adjusted R^2=0.5). The full model including all cognitive variables and their interaction with SiN did not lead to a significant improvement of the model (F(4, 16) = 0.18, p=.945). The interaction suggested that the relationship between

speech-in-noise and cortical thickness was stronger for individuals with better working memory performance within the older group (see Figure 2.12). Thus, for participants with better working memory a thicker cortex in the left superior frontal gyrus was more important to successfully perceive SiN.

Results summary

Older adults performed significantly worse in the SiN task compared to younger adults. SiN performance was correlated with CT in several peri-sylvian and frontal regions. In all of those regions younger adult's cortices were thicker than older adult's. Right pars triangularis and the interaction between age group and left superior frontal gyrus were significant predictors of SiN performance. The interaction suggested that only in older adults superior frontal gyrus was important for SiN perception. A model including SiN score, working memory capacity and their interaction significantly predicted CT in superior frontal gyrus. The interaction suggested that the relation between SiN and CT is stronger for individuals who have higher working memory capacity.

2.2.4 Discussion

The aim of this study was to investigate the relationship between neuroanatomy and SiN perception in older adulthood and to provide insight as to why diverging results have been acquired in previous studies(Giroud, Hirsiger, et al., 2018; P. C. Wong et al., 2010). Correlations between brain morphology (CT and CSA) and SiN were investigated in a sample of younger normal-hearing and older adults with mild hearing loss. The results contribute to the existing literature of the relationship between brain plasticity and SiN perception and suggest a potential explanation for different findings from earlier work.

Age-related differences in auditory perception

The older adults investigated here performed worse in the SiN perception task. This is in line with previous research reporting the same finding (Giroud, Hirsiger, et al., 2018; Helfer & Wilber, 1990; P. C. Wong et al., 2010) and is assumed to reflect difficulties in central hearing in older adults. Results from the multiple regression analysis indicated that PTA did not predict SiN performance but if age was included as a covariate in the model. This provides further evidence that peripheral hearing does not explain SiN performance differences (Cruickshanks et al., 1998; Dubno et al., 1984; Gordon-Salant & Fitzgibbons, 1993; Killion & Niquette, 2000; Souza et al., 2007).

Cortical thinning is evident in older adults

Significant correlations between SiN perception and brain anatomy were only found for CT but not for CSA. In line with this, differences between age groups were only evident for CT, where younger adults were found to consistently have thicker cortices than older adults. These findings corroborate previous observations regarding CT as a predictor of central presbycusis (Giroud, Hirsiger, et al., 2018). Further, a thicker cortex was always related to better performance and older adults cortices were thinner for all regions in consideration. This is in line with the notion that CT, in contrast to CSA, is sensitive to neuroplastic alterations (Giroud, Hirsiger, et al., 2018; Storsve et al., 2014) and the assumed distinguishability of CT and CSA in terms of genetic origin (Meyer et al., 2014; Rakic, 1988, 1995, 2007). Thus, cortical atrophy was evident in the older group for all regions. Further, this result highlight the importance of considering central factors for the investigation and treatment of presbycusis (Giroud, Hirsiger, et al., 2018).

Cortical thickness in auditory and cognition related regions predicts SiN performance

Regions that were significantly correlated with SiN perception ability were found in perisylvian and frontal regions. This adds to the evidence acquired in previous work (Giroud, Hirsiger, et al., 2018; P. C. Wong et al., 2010, 2009). In general, auditory related as well as cognitive regions are thought to be involved in SiN processing (P. C. Wong et al., 2009). Multiple regression analysis revealed that CT in the right pars triangularis and the interaction between age group and cortical thickness in the left superior frontal gyrus were significant predictors of SiN performance.

This suggested that thickness of right pars triangularis was important for SiN perception for both groups. To our knowledge, this region has previously not specifically been related to SiN perception. However, right inferior frontal gyrus has been suggested to be involved in the processing of prosodic speech information (Friederici & Alter, 2004; Kotz et al., 2003; Rota et al., 2009). It has been shown that the prosodic pattern in which a sentence in noise is presented can have an influence on comprehension accuracy (Pinet & Iverson, 2010). Thus, one interpretation for the importance of the right hemispheric pars triangularis for SiN perception would be that prosodic elements of the sentence in noise are important for SiN perception. Additionally, it has been suggested that older and younger adults use prosodic information in similar ways (Wingfield et al., 2000), which could deliver an explanation as to why this region was important for both groups. An alternative interpretation however could be that the right inferior frontal gyrus is involved in attentional control and inhibition (Aron, Robbins, & Poldrack, 2004; Hampshire, Chamberlain, Monti, Duncan, & Owen, 2010), which might point to a role of the right inferior frontal gyrus in the aspects of SiN processing related to executive

functions. However, in light of the present data a final conclusion regarding those two potential functions of the right pars triangularis in SiN perception can not be made. Further work will have to clarify its role in SiN perception.

The relationship between neuroanatomy, SiN perception and cognition in the context of aging and presbycusis

Thickness in left superior frontal gyrus was related to SiN performance only in the older group. A relationship between CT and SiN processing in the same region exclusive to an sample of older adults has been reported by P. C. Wong et al. (2010). These authors suggest that the relationship exists because of the role of the prefrontal cortex in cognition and particularly in working memory. In contrast to Giroud, Hirsiger, et al. (2018), primary auditory regions were not specifically relevant for the older group. A potential explanation for this difference is given by P. C. Wong et al. (2010), stating that cognitive factors play a bigger role when peripheral hearing declines. According to the WHO-classification the sample of older adults investigated here showed mild presbycusis while the group investigated by Giroud, Hirsiger, et al. (2018) did not have peripheral presbycusis which would suggest that the group investigated here was more dependent, whereas the older adults in Giroud, Hirsiger, et al. (2018) were less dependent on cognition. This is in line with research demonstrating that the relationship between cognition, i.e. working memory, and SiN perception is rather weak in listeners with good hearing thresholds (Füllgrabe & Rosen, 2016). Thus, in that sense, frontal compensation mechanisms in speech perception might not be exclusively the consequence of aging but rather might reflect strategies depending on the integrity of the sensory input. In other words, listeners with slight hearing impairment (i.e. the sample investigated hear) use a more cognitive based strategies than individuals with no impairment (i.e. the sample investigated by Giroud, Hirsiger, et al. (2018)) and thus the anatomy of regions related to these cognitive abilities becomes more important.

This interpretation was further supported by the results from the multiple regression analysis including cognition. We found that the interaction between working memory performance and SiN significantly predicted thickness in superior frontal gyrus. The interaction suggested that the relationship between CT and SiN was stronger for individuals who scored higher in the *n*-back task. This finding is in line with work suggesting an involvement of the superior frontal gyrus in working memory processes (Awh et al., 1995; Boisgueheneuc et al., 2006; Braver et al., 1997; Cornette et al., 2001). We interpret this finding in terms of different cognitive strategies used for SiN processing. In our view the results suggest that the use of cognitive strategies depends on the individuals ability in the domain in question. In other words, participants with better cognitive abilities are in a better position to use these abilities to counteract sensory decline and may therefore be more likely to use cognition based strategies in SiN perception. Further, while periph-

eral hearing per se did not predict SiN performance, our results suggest that presbycusis might lead to different strategies in speech perception depending on the integrity of sensory input (Rönnberg, 2003; Rönnberg et al., 2013, 2008) Thus, sensory decline in aging, such as presbycusis, might lead to compensatory strategies based on cognition, but only when cognitive abilities are good enough.

2.2.5 Conclusions

In summary we were able to replicate results obtained in previous studies investigating the relationship between neuroanatomy and SiN perception (Giroud, Hirsiger, et al., 2018; P. C. Wong et al., 2010), suggesting that CT in auditory as well as cognitive regions are predictive of SiN performance. The data presented here also support the notion that CT is a neuroanatomical marker which is tightly related to neuroplastic processes (Giroud, Hirsiger, et al., 2018; Storsve et al., 2014). In addition, we provide first neuroanatomical evidence suggesting different strategies in SiN perception depending on sensory functioning (P. C. Wong et al., 2010). Further, our results suggest that the use of cognitive strategies is also dependent on the cognitive abilities itself.

The present data corroborate and extend previous findings about the relationship between brain anatomy and SiN perception. Cortical atrophy measured by cortical thickness has been shown to be important for SiN performance. Most importantly, our data highlights the need to pay attention to strategies individuals might use depending on their hearing sensitivity or their cognitive abilities.

2.2.6 Limitations

The data presented here are of a cross-sectional nature. Thus, the expressive power of the data presented here in terms of statements about neuroplastic alterations along the lifespan is limited. Longitudinal studies will be needed to get better insights into which changes in brain anatomy are related to changes in SiN processing.

We treated the clusters we found in the whole-brain analysis as monolithic regions. This assumption might not always be true because some clusters might include anatomically and/or functionally different (sub)-regions.

2.3 Article III: When right becomes less right: Neural dedifferentiation during suprasegmental speech processing in the aging brain.

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A similar version of this manuscript has been submitted for publication

Abstract This study combines event-related sparse-temporal acquisition fMRI with structural MRI to investigate elderly participants (n = 26, mean age = 70.64) with age-typical peripheral hearing. While participants were presented with locally time-reversed sentences of varying temporal integrity, they performed an auditory pattern-matching task. The major aim of the study was to find out whether functional lateralization for speech perception according to the 'Asymmetric Sampling in Time' hypothesis (AST) shows a similar pattern in elderly individuals as has been previously observed in younger adults. Our findings indicate that, unlike results previously obtained from younger adults, older individuals did not demonstrate the same pattern of rightward lateralization in response to suprasegmental speech cues in the three auditory regions of interest (ROI), namely Heschl's gyrus, planum temporale and posterior lateral superior temporal gyrus. A frequentist statistical approach did not yield evidence for functional lateralization in the aging brain, and this was corroborated by Bayesian evidence which supported the absence of lateralization in older adults in response to the suprasegmental manipulation. However, a relationship between structural measurements and functional responses demonstrated that individuals with thicker right PT showed less variance in lateralization. This finding suggests that the loss of hemispheric specialization for the processing of rapidly and slowly changing cues in spoken sentences is probably a function of central hearing loss due to age-related brain atrophy. Hence, this study extends the AST hypothesis proposed division of labour between the left and the right auditory cortex during the processing of continuous spoken language in younger adults to a lifespan context.

2.3.1 Introduction

Contrary to the traditional view of language being exclusively a domain of the left hemisphere, it has been observed that patients with right hemispheric lesions show language-related deficits (Heilman, Bowers, Speedie, & Coslett, 1984; Ross, 1981; Ross & Monnot, 2008; Weintraub et al., 1981). The nature of these deficits was that patients struggled to accurately process prosodic aspects of continuous spoken language, namely intonation contour, speech rhythm, intensity and global modulation of the acoustic signal. This has led to the hypothesis that areas in the right auditory-related cortex (ARC) subserve prosodic processing (Ross et al., 2013; Van Lancker, 1997). At the same time, this evidence challenged the long-held belief that the left cortex was the exclusive language-dominant hemisphere. Meanwhile, confluent evidence from neuroscientific studies resulted in the development of frameworks that strongly suggest a bilateral organization of the language-related network. While these models still delineate language as a left dominant faculty, they also acknowledge the contributions of the right perisylvian territory as being essential for the processing of language (Friederici, 2011; Hickok & Poeppel, 2007; Sammler, Grosbras, Anwander, Bestelmeyer, & Belin, 2015; Specht, 2014). The "Asymmetric Sampling in Time" (AST) hypothesis (Poeppel, 2001, 2003) provides an elegant proposal for the division of labour between the left and the right ARC with respect to the processing of continuous spoken language. According to this hypothesis, an initial stage of speech perception relies chiefly on subsegmental, temporal fine-structure (lower γ-band: about 40 Hz) and suprasegmental, temporal envelope information (θ-band: about 4 Hz). Whereas fine-structure information characterizes phoneme representation, the envelope information represents the more global units that constitute prosodic modulation. Furthermore, the AST hypothesis postulates a hemispheric preference in temporal information processing: while the left hemisphere processes primarily fine-structure information, the right hemisphere appears to be preferentially driven by envelope information, that is intonation contour. A number of studies in the last decade have supported this hypothesis and have identified the posterior ARC as the principal processor of temporally-changing speech cues (Boemio et al., 2005; Geiser et al., 2008; Hesling, Clément, et al., 2005; Hesling, Dilharreguy, et al., 2005; Hurschler et al., 2013, 2015; Liem et al., 2014; Meyer et al., 2002; Plante et al., 2002; Zaehle et al., 2004; L. Zhang et al., 2010). Hence, it appears that spoken language has evolved as a bilateral function. However, during the initial stages of pre-lexical processing, there is a lateralized specialization. The result of this computation includes information about the phonemic and prosodic pattern of a continuous spoken utterance. Based on this information, incoming acoustic signals are recognized as a known language and distinguished from unknown languages, music or environmental noise. In addition, this computation lays the foundation for the subsequent higher-order linguistic processes that integrate syntax, grammatical structure

and meaning.

The predictions of this model have so far mainly been tested with younger adults and hence not much is known about the stability of the lateralization patterns in response to temporally-modulating speech sounds across the life-span. Sensory degradation is especially evident in the realm of speech perception, since the likelihood of experiencing sensori-neural hearing loss increases with increasing age (Brant & Fozard, 1990; Cruickshanks et al., 1998; Roth et al., 2011; Wiley et al., 2008). However, loss of hearing sensitivity cannot account for the entirety of speech perception differences between younger and older adults and thus, investigating the 'central' factors of speech processing is also crucial for the understanding of difficulties in speech comprehension typically encountered by older individuals (Peelle & Wingfield, 2016). Taken together, the aging brain is subject to neurofunctional changes in response to alterations of peripherally-driven (e.g. degradation of sensory perception) (Lin et al., 2014; Profant et al., 2014) or centrally-triggered (i.e. cortical atrophy) changes (Reuter-Lorenz & Park, 2014; Sowell et al., 2003). The exploration of spoken language processing in middle-aged adults and seniors is therefore of particular interest because peripheral and central functions are required in order to successfully compute and integrate speech signals and, thus far, little is known about the central contribution to the comprehension of spoken language regarding this tension between age-related hearing and cortical atrophy (Humes et al., 2012).

The present study

The main aim of this study was to shed light on how older adults process spectro-temporal speech information. For this purpose, we applied the paradigm of a previous fMRI study that investigated suprasegmental speech perception in young adults (Liem et al., 2014). The integrity of slowly-changing acoustic cues was parametrically manipulated according to a procedure introduced by Saberi and Perrott (1999). According to the results of our previous fMRI study, lateralization to the right ARC increased with parametrically increasing temporal integration window length, supporting the idea of a preference of the right ARC for suprasegmental speech information. We tested the predictions of the AST hypothesis for suprasegmental speech processing in a sample of older adults without considerable peripheral hearing loss primarily to evaluate the effect of central losses on spoken language comprehension.

If this pattern of lateralization persists across the lifespan, one would expect to see the same kind of lateralization pattern in older adults as seen in younger adults. If this specific kind of processing, however, is subject to lifespan changes, we would expect to see a different pattern which could indicate either a switch of lateralization towards the other hemisphere or a loss of asymmetric processing. In light of results from other work investigating lateralization in speech processing (Bellis et al., 2000) and from other

cognitive domains (Cabeza, 2002; Reuter-Lorenz & Park, 2014), it seems, however, more likely that lateralization decreases.

Regarding structural plasticity, cortical thickness (CT) of the human brain is subject to age-related changes (Salat et al., 2004; Thambisetty et al., 2010) and there is initial evidence that the structure of the right auditory cortex plays an important role in the maintenance of speech processing abilities at an older age (Giroud, Hirsiger, et al., 2018). In particular, CT of right ARC regions was positively related to performance in various auditory functions, meaning that participants with a thicker cortex in those regions scored higher in the tasks. This observation suggests that, in the context of age-related central hearing loss, neuroplastic processes which affect the right ARC are associated with behavioral performance. Interestingly, findings regarding cross-domain plasticity also suggest that the right ARC, specifically the PT, is involved in neuroplastic reorganization processes (Shiell, Champoux, & Zatorre, 2016). On a behavioural level, older adults, compared to younger individuals, rely more strongly on suprasegmental speech information (Wingfield et al., 2000) which, according to the AST model, is preferentially processed by right hemispheric non-primary auditory regions. Taken together, these findings all point towards a crucial role of the right ARC for central speech processing in older adulthood.

Currently, there is a debate around what the specific age-related changes in patterns of neural activation may mean for the individual's performance, or their ability in a given task or task domain at hand. In general, there are two competing hypotheses which make different predictions for the relation between lateralization patterns and behavioural performance. On one hand, changes in lateralization in old age could represent the brain's attempt to compensate for deficits in the domain of the task by recruiting additional areas of the brain (Cabeza, 2002). Along these lines, less lateralized processing would be expected to lead to a better performance, since an increased recruitment of contralateral homologue areas would indicate that more neural resources are available. It should be noted that this hypothesis has been formulated with respect to prefrontal activation; however, to the best of our knowledge, there is no evidence yet that would rule out the possibility of a similar mechanism for auditory-related areas. Thus, we consider compensation as one candidate mechanism that may account for changes in lateralization during elementary speech processing following age-related central hearing loss. An alterative hypothesis states that changes in lateralization are a consequence of neural dedifferentiation (Baltes & Lindenberger, 1997; S.-C. Li et al., 2004), meaning that neural responses to stimuli become less specific in older adulthood. In other words, the human aging brain buys robustness at the expense of specialization. With respect to spoken language comprehension, this would manifest in a less specified lateralization pattern which could be characterized by a larger variation in functional lateralization. Increases in dedifferentiation in aging have been linked to decreases in cognitive abilities (S.-C. Li,

Lindenberger, & Sikström, 2001b; J. Park, Carp, Hebrank, Park, & Polk, 2010). Thus, if increased symmetric processing is a means of compensation, one would expect participants with a less lateralized activation pattern to perform better in a behavioural task. Alternatively, if reduced lateralization accompanies neural dedifferentiation, one would expect individuals who show less variation in their neural response pattern to perform better in a behavioural task. Hence, a secondary aim of the study was to investigate how the lateralization pattern in older adults fitted to current alternative frameworks of neurocognitive aging, namely compensation versus dedifferentiation. In order to test the predictions made by each hypothesis, mean lateralization across conditions and inter-condition standard deviation (ICS) were calculated and used to predict mean behavioural performance in the in-scanner task.

Lastly, it was of interest to find out how age-related cortical atrophy affected temporal lobe neural functioning, given that gray matter is subject to lifespan cortical thinning (Fjell & Walhovd, 2010; Fjell et al., 2009; Sowell et al., 2003), in particular with respect to central hearing loss (Lin et al., 2014). Despite the fact that only little is known about this relationship so far, there is at least initial evidence that demonstrates a direct link between brain morphology and auditory brain function (Greve et al., 2013; Liem, Zaehle, Burkhard, Jäncke, & Meyer, 2012) as well as performance (Giroud, Hirsiger, et al., 2018). Thus, another secondary aim was to investigate whether measures of cortical anatomy, namely CT and cortical surface area (CSA), were related to brain function by correlating them with mean lateralization and ICS. Investigating the interplay between brain structure, function and behavioural outcome in relation to aging thus seems to be a promising approach to a better understanding of the complex nature of the aging brain.

In summary, given that older adults tend to show less lateralization in general, we expected that older adults would show a bilateral pattern of neural responses to suprasegmental speech information, and that this could best be explained by a loss of specificity of neural responses in older adulthood and not by compensation. Furthermore, we assumed a relationship between structure of the brain and brain function. In particular, we expected that CT especially would be a relevant anatomical parameter related to neural function in older adulthood.

2.3.2 Methods

Participants

Twenty-six individuals (13 female, M_{age} = 70.64, SD = 4.66) participated in the experiment. Participants were native (Swiss-)German speakers. They did not report any history of psychological or psychiatric disorder as well as no history of brain injuries. None of the participants reported speech and/or hearing impairments and none of them were

using hearing aids. Pure-tone average (PTA) was measured for 500, 1000, 2000 and 4000 Hz for each ear, individually. Age-typical hearing loss was evident with pronounced elevation of thresholds for higher frequencies (see Figure 2.13).

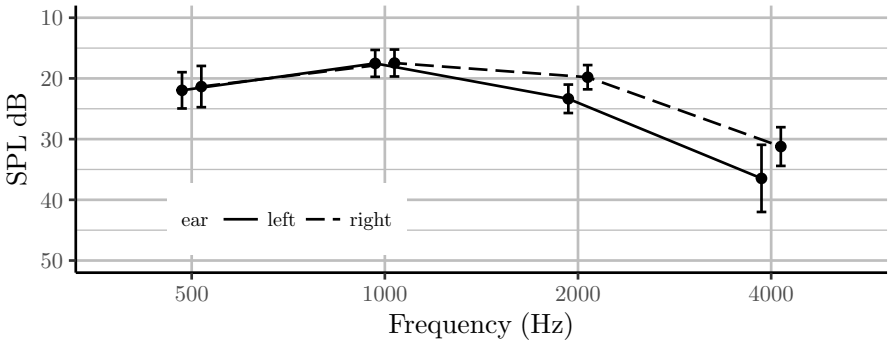

Figure 2.13. Pure-tone thresholds shown for each ear, separately. Error bars indicate 95% within subject CIs.

PTA asymmetries did not exceed 14 dB SPL in each participant. In order to measure central hearing, participants' speech in noise intelligibility performance was assessed using the Oldenburg Sentence Test (OLSA) (Wagener et al., 1999a, 1999b, 1999c). This test is considered as a suitable device that measures substrates of central hearing loss. It actually gives an indication of how well individuals are able to understand spoken language in the presence of background noise. Using an adaptive procedure, the OLSA assesses the difference in speech and noise level by which an individual is still able to understand 50% of the words from a spoken sentence. On average, participants were able to understand 50% of the words if noise was 2.736 (SD = 2.164) dB SPL above speech SPL. These values indicate that in the sample under investigation here central hearing loss is evident (Giroud, Hirsiger, et al., 2018). All of the participants were right-handed (Annett, 1970) and had no musical training. Participants were screened for cognitive impairment by means of the Mini Mental State Examination (MMSE (Folstein et al., 1975)) and only participants that scored at least 27 points were included. Volunteers gave written informed consent prior to data collection. The study was approved by the Ethics Committee of the canton of Zurich (application no. KEK-ZH-Nr. 2015-0541).

Stimuli

The same set of stimuli as used by Liem et al. (2014) was used here. Spoken German sentences were locally time-reversed which results in a decrease of availability of TE information along with increasing segment length (Saberi & Perrott, 1999; Walker, Ahmed, & Schnupp, 2008). Segment lengths were different between conditions (0, 100, 150, 200, 250 ms) resulting in six experimental conditions consisting of a total of one hundred and eighty sentences to create conditions of differential suprasegmental temporal integrity. Sentences were split into segments and then locally time-reversed. Since

time-reversing segments leads to temporal discontinuities resulting in audible artifacts at the border of two segments, overlapping cosine windows were utilized. This was done via a procedure introduced by Walker et al. (2008) and resulted in artifact free stimuli (cfg. Liem et al., 2014). In addition, unaltered sentences (0 ms) were presented. The duration of the sentences ranged from 2.2 to 3.5 s (M $\frac{1}{4}$ 2.9 s). The conditions did not differ with regards to sentence duration, stimulus intensity, and intonation contour (for further information see Liem et al. (2014)).

Design and procedure

Prior to MRI data collection participants were introduced to the task outside the scanner. Stimuli were presented to the participants via sound attenuating (30 dB) MR headphones (NordicNeuroLab, Bergen, Norway) with a flat frequency response between 8Hz and 35kHz and equipped with high precision electrostatic transducers. Participants were asked to listen to a sentence through the headphones to ensure stimuli were audible to the participants and to adjust the volume if necessary. Participants were instructed to keep their eyes open during the fMRI task and to look at a fixation cross via a coil-mounted mirror. After the presentation of each sentence a probe stimulus was presented followed by the response phase. Stimulus delivery took place during scanner silent intervals while participants responded during image acquisition (see Liem et al., 2014, for more information). Probe stimuli were short snippets that were taken either from the preceding (unmanipulated) sentence or from a different sentence and participants were asked to indicate whether the snippet was part of that sentence or not by pressing the according button on a response box. Each condition (0, 100, 150, 200, 250ms) consisted of 36 trials recorded across two runs. In addition to these conditions, in order to control for motor-related brain activity, participants were asked to respond to a baseline condition where no stimuli were presented by randomly pressing a button on the response box. This resulted in a total of 216 trials. Within each experimental condition, 50% of the probe stimuli matched the the preceding sentence. PTAs and speech in noise performance were acquired in an additional session.

MRI data acquisition

MRI sessions were performed at the University Hospital Zurich on a Philips 3T Ingenia system (Philips Medical Systems, Best, the Netherlands) using a 15-channel Philips Sense head coil. Functional images were collected by single-shot echo-planar imaging using a clustered-sparse acquisition scheme (ref). For each trial three volumes were recorded (echo planar imaging, 15 transversal slices, in-plane resolution = 1.72 x 1.72 mm, slice thickness = 4mm, inter-slice gap = 2mm, matrix size = 128 x 128, field of view [FOV] = 220 x 220 mm, cluster-onset asynchrony [COA] = 7.5s, acquisition time [TA] = 1s,

echo time [TE] = 35ms, flip angle = 68°) which resulted in 648 functional images in total. The functional images were recorded along the anterior posterior commissure and covered the entire sylvian and perisylvian cortex. Before the functional data acquisition a T1 weighted structural image was recorded (turbo field echo, 160 saggital slices, in-plane resolution = 0.94 x 0.94 mm, slice thickness = 1 mm, matrix size = 256 x 256 mm, FOV = 240 x 240 mm, repetition time [TR] = 8.15 ms, TE = 3.74 ms, flip angle = 8°).

MRI data analysis

The T1 images were segmented using Freesurfer (5.3.0; `http://surfer.nmr.mgh.harvard.edu/`) in order to get individual regions of interest for use in the functional analysis. Cortical parcellation was done according to the aparc.a2009s parcellation (Destrieux et al., 2010). This resulted in individual, anatomically defined ROIs of the HG, PT, pSTG (see Figure 2.14). Functional data analysis was performed with SPM 12 (`http://www.fil.ion.ucl.ac.uk/spm/software/spm12/`) in a Matlab R2016b environment. Functional images were realigned and smoothed with an isotropic 6 mm FWHM Gaussian kernel. Contrast between all the conditions and the control conditions were calculated using general linear modeling. Thereby each stimulus was modeled as an event and the hemodynamic response was approximated using a boxcar function (finite impulse response, 1st order, window length = 3s). According to Zaehle et al. (2007) and Liem et al. (2014), two regressors of no interest were included in the analysis to account for T1 signal decay within single acquisition clusters. ROI analysis was performed in native space and beta values were extracted from the individual ROIs of each participant. Only activated voxels (i.e. voxels with a positive beta) were used for the calculation of the lateralization index ($LI = \frac{LH-RH}{LH+RH}$). Accordingly, positive values indicate lateralization to the left and negative values indicate rightward lateralization and values can range from -1 to +1. Mean lateralization over all conditions was calculated as a measure of overall lateralization and ICS was simply the standard deviation of the LI over all conditions.

(a) Right hemispheric ROIs *(b)* Left hemispheric ROIs

Figure 2.14. ROIs projected on the average inflated brain of all participants. Red = HG, green = PT and blue = pSTG.

Statistical analysis

Statistical analyses were performed using R software (R Core Team, 2017). Frequentist ANOVAs were calculated with the afex package ((Singmann, Bolker, Westfall, & Aust, 2018), version: 0.20.2). Effect sizes are reported as partial eta squared to enable comparison with the effect sizes reported by Liem et al. (2014). Furthermore, to asses the relative strength of evidence for two competing hypotheses (i.e. the null versus the alternative hypothesis), Bayes factors (BF (e.g. Dienes, 2014; Kruschke, 2011; Lee & Wagenmakers, 2005; Rouder, Speckman, Sun, Morey, & Iverson, 2009)) were computed using the "BayesFactor" package ((Morey & Rouder, 2015), version: 0.9.12.4.2). BFs can take values from zero to infinity whereby higher values indicate stronger support for the respective hypothesis. A main advantage of BFs is that it is possible to quantify evidence for the null hypothesis and thus indicate how likely it is that an effect is absent (Dienes, 2014). Using this approach here seems appropriate since in terms of lateralization the null hypothesis (i.e. that there is no lateralization) is theoretically meaningful. Specific effects were tested by comparing models including the effect versus the same model without the effect. Evidence in favour of including an effect of interest is denoted as BF_{10} and evidence against the inclusion of the effect–which is the inverse of BF_{10}–is denoted BF_{01}. Estimates of model coefficients of interest were obtained through sampling 10'000 draws from the posterior distribution of the full model. The mean of the posterior distribution and its corresponding 95% highest density interval (HDI) are reported. Priors were chosen as the default prior implemented in the "BayesFactor" package, which is a Cauchy distribution with a medium scaling factor of $r = 0.707$. To assess the sensitivity of the results to the prior, analyses were rerun with a wider ($r = 2.00$) and a narrower ($r = 0.50$) prior. For both of these priors the conclusions remained the same.

2.3.3 Results

In-scanner task

Frequentist one-way repeated measures ANOVA revealed a significant effect of segment length on percent correct responses ($F(3.687, 88.478) = 25.002$, $p<.001$, $\eta^2 p = 0.51$). Similarly, the Bayesian analysis revealed that there was decisive evidence in favour of an effect of segment length on percent correct responses ($BF_{10} = 2.589 \times 10^{-12} \pm 0.009\%$).

In-scanner task performance is displayed in Figure 2.15. This indicates that performance decreased with increasing segment length. Means and standard deviations of percent correct responses for each condition can be found in 2.3.9, Table A1.

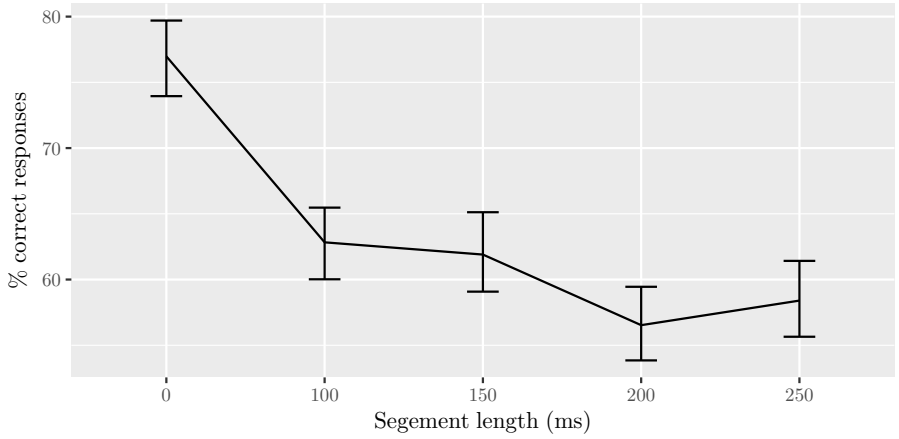

Figure 2.15. Effect of segment length on percent correct responses. Error bars represent the 95% highest density intervals (HDI) plotted around the mean as the point estimate drawn from the posterior distribution.

Lateralization

To test whether BOLD signals collected from ROIs were sensitive to the temporal manipulations of the sentences, one-way repeated measures frequentist ANOVAs with lateralization index as the dependent variable and segment length as the predictor were calculated for each ROI. There was no significant effect for any of the three ROIs (HG: $F(3.66, 91.488) = 1.071$, $p = .373$, $\eta^2p = 0.041$, PT: $F(3.298, 82.458) = 1.547$, $p = .205$, $\eta^2p = 0.058$, pSTG: $F(2.648, 66.193) = 2.391$, $p = .084$, $\eta^2p = 0.087$). To quantify the relative evidence for the null and the alternative hypotheses, Bayesian linear mixed models with lateralization index as dependent variable and segment length as predictors were calculated. Subjects were modeled as random factors to asses for the repeated measures nature of the design. BFs were calculated by comparing the model including condition as factor against the intercept-only model. There was substantial evidence for the absence of lateralization in HG ($BF_{01} = 18.31 \pm 0\%$) and PT ($BF_{01} = 8.73 \pm 0.01\%$) and anecdotal evidence for pSTG ($BF_{01} = 2.38 \pm 0\%$) (see Figure 2.16).

This indicates that different segment lengths did not have an influence on the hemispheric lateralization in all of the three ROIs. Means and standard deviations of raw data (mean beta values) can be found in 2.3.9, Table A2.

Function and performance

Mean LI was calculated as the mean lateralization over all conditions and ICS was calculated as the standard deviation over all conditions. To assess whether mean lateralization and variation in lateralization contributed to the performance in the pattern-matching task, linear models for each ROI and each measurement were calculated, controlling for age, gender, hearing threshold and hearing asymmetry.

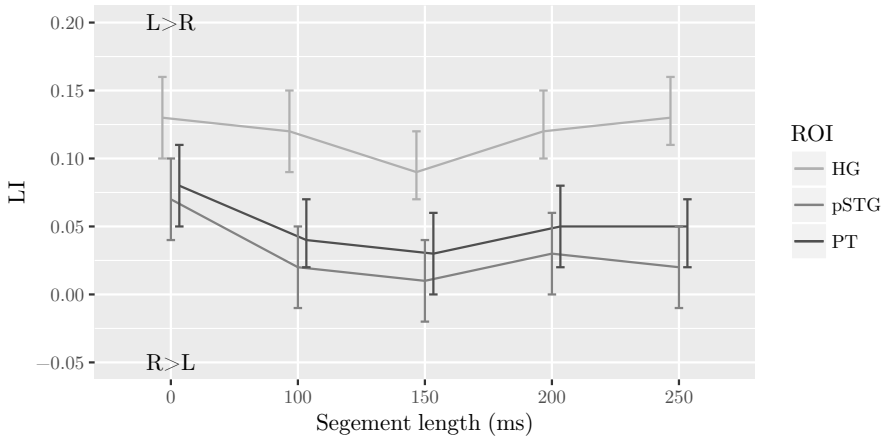

Figure 2.16. Effect of segment length on lateralization for the three ROIs. Error bars represent the 95% highest density intervals (HDI) plotted around the mean as the point estimate drawn from the posterior distribution.

In a first step, a frequentist linear model without the predictor of interest (i.e. mean lateralization or ICS), including hearing threshold, hearing asymmetry, gender and age was calculated. The results indicated that this model explained 50.1% of the variance and that the model was a significant predictor of performance ($F(4, 21) = 5.276$, $p = .004$). While hearing threshold contributed significantly to the model ($B = -0.682$, $p<.001$), hearing asymmetry ($B = 0.401$, $p = .122$), gender ($B = 4.42$, $p = .124$) and age ($B = 0.66$, $p = .077$) did not.

Adding mean lateralization from any of the ROIs to the model did not lead to more explained variance (HG: $\Delta R^2 = 0.004$, $F(1, 20) = 0.143$, $p = .71$, PT: $\Delta R^2 = 0.003$, $F(1, 20) = 0.107$, $p = .747$, pSTG: $\Delta R^2 = 0.012$, $F(1, 20) = 0.511$, $p = .483$).

However, adding ICS in lateralization in PT or pSTG to the model significantly explained more variance in performance (HG: $\Delta R^2 = 0.074$, $F(1, 20) = 3.512$, $p = .076$, PT: $\Delta R^2 = 0.165$, $F(1, 20) = 9.895$, $p = .005$, $B_{PT} = -92.824$, pSTG: $\Delta R^2 = 0.121$, $F(1, 20) = 6.427$, $p = .02$, $B_{pSTG} = -62.697$). Overall, the full model including ICS of PT was able to account for 66.6% of the variance in performance and the full model including ICS of pSTG was able to account for 62.3% of the variance in performance.

Bayesian linear models were calculated with mean percent correct responses as the dependent variable and age, mean hearing threshold, mean hearing asymmetry and gender and the variable of interest (mean of LI or ICS of LI for each ROI) as predictors. BFs were calculated by comparing the model including the variable of interest with the model omitting the variable of interest. In the case of mean lateralization evidence favoured the null model, while for ICS of lateralization the alternative model was favoured for all ROIs (Table 2.7). Out of all these models, the most probable model includes the PT as predictor indicating that the data are around 10 times more likely to be observed under a model that includes the PT. The standard deviation of lateralization was negatively re-

lated to in-scanner performance, indicating that participants with smaller SD performed better in the in-scanner task (Figure 2.17).

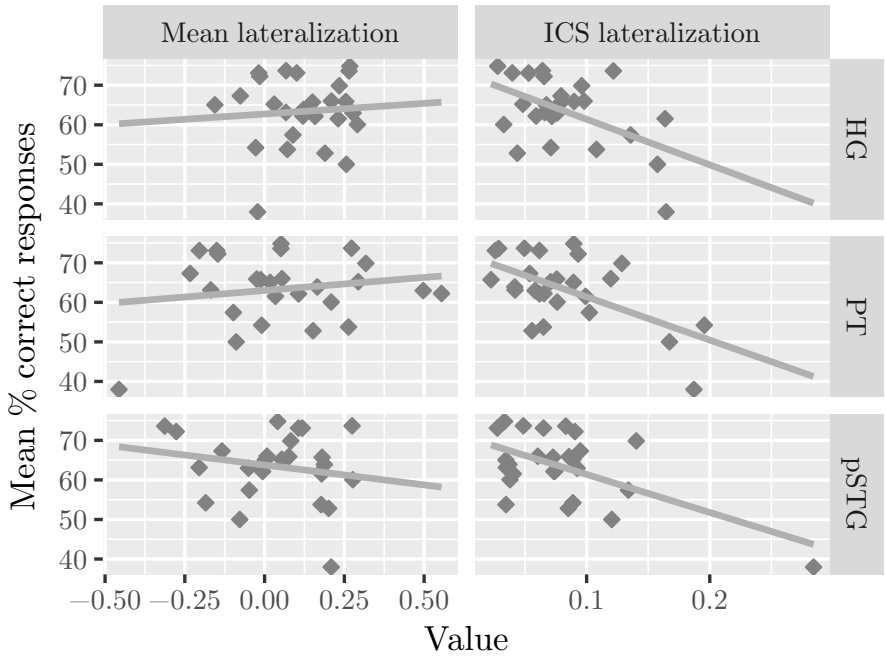

Figure 2.17. Relation between mean lateralization and mean performance (top) and ICS and mean performance (bottom). Lines indicate the slope estimates of an OLS regression.

Table 2.7

Regression table: activation and performance.

	Posterior mean	BF10	BF01	error %	95% HDI
ICS lateralization					
HG	-52.2	1.55	0.64	± 1.3e-05	[-1.2e+02; 1.5e+01]
PT	-77.9	10.76	0.09	± 3.6e-05	[-1.3e+02; -1.6e+01]
pSTG	-51.2	3.94	0.25	± 2.3e-05	[-9.9e+01; -1.1e+00]
Mean lateralization					
HG	3.4	0.47	2.13	± 1.2e-05	[-1.8e+01; 2.4e+01]
PT	-1.7	0.46	2.16	± 1.2e-05	[-1.3e+01; 1.1e+01]
pSTG	-4.8	0.54	1.85	± 1.2e-05	[-2.2e+01; 1.1e+01]

Results are controlled for the effect of age, gender and hearing loss. ICS = inter condition standard deviation, HG = heschl's gyrus, PT = planum temporale, pSTG = posterior superior temporal gyrus.

Function and structure

Since no relationship between mean lateralization and performance was found and ICS of the PT was the strongest predictor for behavioural outcome, the function-structure

analysis was subsequently restricted to ICS of the PT. In order to investigate the relationship between anatomy and function, frequentist and Bayesian linear models with CT and CSA as predictors of variability in PT were calculated. Only on inclusion of right hemispheric CT could a significant regression equation be found ($F(1, 24) = 7.715$, $p = .01$), explaining 24.3% of the variance in ICS. Regression models including left hemispheric CT and CSA and right hemispheric CSA did not reach significance (CT l: $F(1, 24) = 1.338$, $p = 0.259$, CSA r: $F(1, 24) = 0.245$, $p = 0.625$, CSA l: $F(1, 24) = 0.745$, $p = 0.397$). BFs were calculated by comparing the model including the anatomical measure of interest against the intercept-only model. Results are presented in Table 2.8. The sole evidence in favour of a model including the anatomical measure of interest was found for CT of the right PT, indicating that individuals with a thicker right-hemisphere cortex showed less variability in lateralization than individuals with a thinner cortex (see Figure 2.18).

Table 2.8
Regression table: ICS and anatomical measures.

	Posterior mean	BF10	BF01	error %	95% HDI
CT r	-0.09	4.96	0.2	± 5.4e-06	[-1.8e-01; -1.5e-02]
CT l	-0.04	0.59	1.7	± 1.1e-05	[-1.3e-01; 4.2e-02]
CSA r	0.00	0.40	2.5	± 1.7e-05	[-2.0e-04; 1.0e-04]
CSA l	0.00	0.48	2.1	± 1.2e-05	[-2.0e-04; 1.0e-04]

CT = cortical thickness, CSA = cortical surface area, r = right hemisphere, l = left hemisphere.

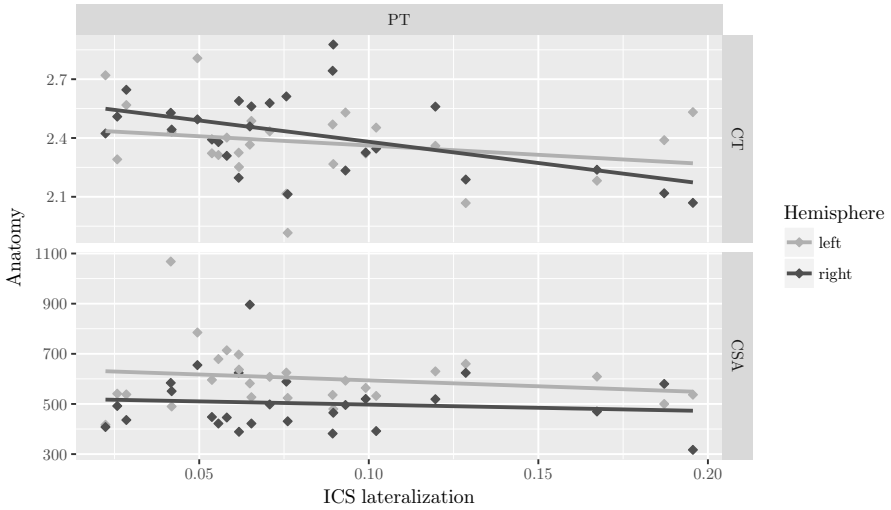

Figure 2.18.
Relation between CT (top panel) and CSA (bottom panel) and variability. Lines indicate the slope estimates of an OLS regression.

Results summary

Neuronal responses in older adults did not shift to either hemisphere in response to suprasegmental manipulation of spoken language. ICS of lateralization, but not mean lateralization, was related to the in-scanner pattern-matching task performance. More specifically, less variation in lateralization across condition was related to better in-scanner task performance. CT in the right PT was related to ICS of the PT, indicating that a thicker right ARC was related to less variation in lateralization across conditions.

2.3.4 Discussion

A core aspect of daily life is being capable of taking part in spoken communication. It is therefore understandable that hearing loss is reported to be associated with a remarkable decrease in the quality of life, particularly in elderly individuals (Arlinger, 2003; Vannson et al., 2015). Hence, peripheral and central hearing loss are key components of human brain aging. The latter especially remains underinvestigated but the presently burgeoning field of Cognitive Hearing is beginning to elucidate the complex interplay between various forms of hearing loss, age-related cognitive decline and atrophy of brain morphology (Giroud, Hirsiger, et al., 2018; Humes et al., 2012; Peelle & Wingfield, 2016). More precisely, uncovering the interplay between these factors is a complex endeavour, one with the ultimate goal of gathering knowledge about how older adults could stabilize and maintain communicative functions of daily life despite sensory, cognitive and neural decline. In terms of such sensory decline, age-related peripheral hearing loss is part of the normal aging processes and is traditionally characterized by elevated hearing thresholds (Brant & Fozard, 1990; Cruickshanks et al., 1998; Roth et al., 2011; Wiley et al., 2008). However, differences in hearing status are not sufficient to explain all the differences in speech comprehension between older and younger adults (Humes et al., 2012). On the one hand, cortical atrophy and decline in neural functioning could contribute to the speech perception difficulties experienced in older adulthood (Giroud, Hirsiger, et al., 2018). On the other hand, it cannot be ruled out that the observed pattern could also work in a compensatory way as it has been described for other cognitive domains (e.g. Cabeza, 2002; Reuter-Lorenz & Park, 2014) to counteract functional decline . Thus the main goal of this study was to contribute to the understanding of central factors of speech processing in older adulthood. By investigating suprasegmental speech processing, we aimed to shed light on functional hemispheric lateralization. Further, this lateralization was considered with reference to competing theories of neurocognitive aging by examining the relationship between neural activation and behaviour. Lastly, linking neural activation with measures of brain morphometry provided insight into the relationship between cortical atrophy and neuronal functioning.

No lateralization in the processing of temporal speech information

Stimulus modulation did not have an effect on hemispheric lateralization in the ROIs we investigated. Moreover, Bayesian analysis revealed that the null model of no lateralization was more likely for all three ROIs and can thus be interpreted as evidence against a sensitivity of lateralization in the three ROIs to supratemporal speech information in older adults. This result is in line with earlier work reporting reduced lateralization of early auditory processing for CV syllables in older compared to younger adults (Bellis et al., 2000). Similar to the body of studies reporting reduced lateralization in prefrontal areas for working memory paradigms (Cabeza, 2002; Reuter-Lorenz & Park, 2014), we observed symmetrical processing in temporal areas. Regarding the postulated respective preferences of the left and right ARC for the processing of temporal speech information as advocated by the AST hypothesis (Poeppel, 2003), the present results suggest that this model cannot be generalized directly to older populations and that an extension of the model is probably needed. Using a research design that is not longitudinal, statements about the course of development in relation to lateralization of language functions along the lifespan are of course limited. However, the results presented here clearly indicate the need for further investigation into the central processing of temporal speech information with respect to aging, ideally using longitudinal designs in order to accurately describe changes in neural (lateralization) patterns in auditory processing with advancing age.

Compensation or dedifferentiation?

The data presented here do not favour an interpretation of reduced lateralization of speech processing in older adults as a result of recruitment of additional neuronal resources and thus as a compensatory process (Cabeza, 2002). According to these models, individuals who are able to recruit homologue areas of the contralateral hemisphere should perform better because additional neuronal resources are available to them. However, the data are relatively inconclusive, since they only suggest that it is just slightly more likely that mean lateralization and performance are not related than that they are. Further, these frameworks are based on research on working memory paradigms. Our present study is the first that addresses the issue of age-related changes in lateralization in the context of continuous spoken language comprehension.

Evidently, the extent of variation in lateralization was related to the behavioural outcome, mainly in the PT and to a lesser extent in the pSTG. Participants whose lateralization pattern changed less between conditions performed better than those whose did change more strongly. This is in line with hypotheses that suggest that more stable neuronal representations are related to better performance in older adulthood (S.-C. Li et al., 2001b; J. Park et al., 2010). It should be noted that in this case variability was not measured as the variability of the brain response per se but as the stability of lat-

eralization between conditions. Further, it is not entirely clear whether more variability in neuronal activation always has detrimental effects on performance. Evidence on the voxel-level suggests that more variability can also be beneficial for performance (Garrett, Kovacevic, McIntosh, & Grady, 2011). Nonetheless, these results highlight the significance of variability-based measures for the investigation of the relationship between the aging brain and performance in older adulthood and can be interpreted in the context of a dedifferentiation framework. In summary, the data presented here suggest neural dedifferentiation as the more likely mechanism accounting for behavioural differences between older adults. This would imply changes at the functional and structural level with the latter primarily affecting gray matter thickness as this parameter is most likely to reflect plastic alterations.

Thicker cortex in PT is related to less dedifferentiation

We tested whether cortical anatomy was related to stability of lateralization in PT. Out of the tested anatomical measures only CT in the right PT was related to variation of the neuronal response. It has been suggested that CT and CSA have different genetic origins (Panizzon et al., 2009; Rakic, 1988, 1995, 2007) and that it is mainly CT that is susceptible to training or to plastic alterations across the lifespan (Bermudez et al., 2008; Engvig et al., 2010; Storsve et al., 2014). This proposition is also true for the results presented here. Individuals with a thicker cortex in the PT show a more stable lateralization pattern. Interestingly, this observation was only the case for the right but not for the left hemisphere. The finding could be an indication of the importance of right ARC integrity for hearing and speech perception (Giroud, Hirsiger, et al., 2018) and may specifically point towards the right PT as an important area for structural plasticity. Apart from one study that reported a negative relationship between cortical volume and dedifferentiation in the visual domain (Voss et al., 2008), there is little work investigating the relationship between dedifferentiation and brain structure and as a result concrete hypotheses are lacking. It is thus suggested that this issue should be further investigated in order to clarify the relationship between brain structure and neural dedifferentiation. Without longitudinal measurements, it is not possible to indicate whether the relationship between CT and dedifferentiation should be classified as stabilization or compensation. It might be that individuals who show less cortical atrophy–and thus have a thicker cortex–are less susceptible to deficits in speech perception. Alternatively, a thickening of the cortex could be conceived as an appropriate response to impaired speech perception. While the entirety of the present literature favors the first view, it cannot be completely ruled out that the last option could hold true. As long as only cross-sectional data are available, a final answer cannot be provided.

2.3.5 Conclusion

The findings presented here provide insight into the neuronal processing of temporal speech information in older adults with respect to hemispheric lateralization. More specifically, older adults seem to lack the hemispheric specialization observed in younger adults when processing temporal speech cues. In light of the reports of cortical thinning in older adults, it could be argued that this might be a function of central hearing loss due to age-related brain atrophy. Overall, our results contribute to a better understanding of age-related changes in speech processing and age-related (central) hearing loss.

2.3.6 Conflicts of interest

We state that there are no competing interests.

2.3.7 Declaration of interests

None.

2.3.8 Acknowledgments

We thank Franziskus Liem for providing us with the stimulus material and relevant code for setting up the experimental paradigm, as well as for helpful comments. This study was funded by the Swiss National Science Foundation (SNF, Grant no. 105314_152905 to MM). The sponsor did approve of the general study design but did not play any role in the collection, analysis and interpretation of the data. During the work on his dissertation, Matthias Keller was a pre-doctoral fellow of LIFE (International Max Planck Research School on the Life Course; participating institutions: MPI for Human Development, Humboldt-Universität zu Berlin, Freie Universität Berlin, University of Michigan, University of Virginia, University of Zurich). Financial support by the Jacobs Foundation helped to conduct this research.

2.3.9 Appendix A

Table A1

Means and SD of percent correct responses for each Condition.

Segment length (ms)	M	SD
0	77.4	10.35
100	62.9	14.26
150	62.7	11.17
200	57.2	8.29
250	58.3	10.47

M = mean, SD = standard deviation.

Table A2

Means and SD of mean beta values for each Condition.

Segment length	0		100		150		200		250	
	M	SD	M	SD	M	SD	M	SD	M	SD
Regions										
LH										
HG	1.32	0.499	1.325	0.492	1.323	0.525	1.393	0.461	1.264	0.478
PT	1.14	0.605	1.028	0.476	0.968	0.463	1.026	0.459	0.982	0.515
pSTG	1.64	0.759	1.296	0.602	1.155	0.537	1.243	0.576	1.172	0.564
RH										
HG	1.04	0.522	1.083	0.594	1.118	0.501	1.126	0.539	1.001	0.462
PT	1.01	0.586	0.944	0.448	0.956	0.534	0.929	0.429	0.881	0.433
pSTG	1.37	0.597	1.160	0.411	1.119	0.508	1.099	0.380	1.093	0.512

HG = heschl's gyrus, PT = planum temporale, pSTG = posterior superior temporal gyrus, LH = left hemisphere, RH = right hemisphere.

Chapter 3

Discussion

The main goal of this thesis was to provide insight into the neuronal speech processing in older adults and thus offering perspectives on hearing and speech comprehension beyond hearing thresholds. In particular, functional and anatomical features of the aging brain were shown to be important for speech processing and potential candidates for explaining variability in speech perception in older adulthood, beyond hearing thresholds, were identified. In this chapter the key findings from the empirical part will be reviewed and summarized. Results will be discussed in the context of temporary frameworks and hypotheses relevant to the pertaining result. Open issues from each study will be identified and newly arising questions will be discussed. Finally, an outlook of future perspective will be presented.

3.1 Summary of the results

In the first article of this thesis (Giroud et al. (n.d.), see Chapter 2.1.6) the neuronal processing of prosodic speech information on the word level was studied. The MMN, as an electrophysiological indicator of automated auditory processing, was investigated in a group of older and a group of younger individuals. MMNs were recorded in response to hearing words with differently positioned stress.

The results paralleled findings from behavioural studies (Wingfield et al., 2000), indicating that older adults were more sensitive to word stress than older adults. In addition, discrimination accuracy of pitch, measured in a behavioural task, was related to CT in right hemispheric auditory areas. Within the older group, individuals with thinner cortices performed worse in this task.

Thus, we concluded that first, older adults are more sensitive to prosodic speech information, not only on the behavioural level but also on the neural level. And, second, brain anatomy in auditory areas is related to speech perception in older adults, where cortical atrophy has a detrimental effect.

In the second article of this thesis (Keller, Giroud, and Meyer (n.d.), see Chapter 2.2.6) the relation between SiN perception, brain anatomy and cognition was investigated. Correlations between measures of brain anatomy and SiN performance in a group of younger normal hearing and older adults with mild presbycusis were calculated. We found that within correlated regions, CT of the superior frontal gyrus was related to SiN performance, but exclusively in the older group. This relationship was modulated by WM capacity, indicating that the relationship between SiN and CT in this region was strongest for individuals with high WM capacity.

This study provided corroborative evidence for CT as a key anatomical measure for the investigation of neuroplastic processes in a lifespan context. In other words, neuroplastic processes manifest themselves in the thickness of the cortex rather than in the surface area. Further, the results suggest that for individuals with sensory decline, cognitive abilities become more important for speech perception, as indicated by the importance of the superior frontal gyrus for SiN performance in the older group with mild hearing loss.

Lastly, the observations from *study II* indicate that this cognitive compensation strategy, although increasingly important for individuals with presbycusis, is most relevant for individuals with good cognitive capacity. That is, older adults with presbycusis likely use cognitive strategies to understand speech, but only when these cognitive abilities are sufficiently maintained in old age.

In the third article of this thesis (Keller, Neuschwander, and Meyer (n.d.) see chapter 2.3.9) the neurofunctional anatomy of suprasegmental speech processing in older adults was investigated. A group of older participants underwent fMRI testing while performing an auditory pattern-matching task. While this paradigm has been shown to elicit a lateralized pattern of neural responses with increasing suprasegmental processing in the auditory cortex in younger adults, this was not the case in the older adults, where we found that the suprasegmental manipulation did not lead to changes in lateralization.

Notably, performance in the in-scanner task could be best explained by the variability in lateralization pattern over conditions and not by mean lateralization per se. Furthermore, variability in the hemodynamic response was related to cortical thickness in PT of the right hemisphere. In line with observations made in previous studies older adults did show a bilateral pattern of neural responses. Hence, assumptions of models of speech perception based on observation from young populations cannot be directly transferred to older samples.

This reduction of lateralization in older adults could not be explained by a compensatory mechanism of older adults. Rather, the results obtained in *study III* suggest that this pattern of hemodynamic responses in older adults reflects neural dedifferentiation processes. Finally, individuals with a thicker cortex in the right PT showed less dedifferentiation and also performed better in the pattern-matching task.

3.2 Implications

The results of this thesis have several implications. These implications will be discussed in this section from a theoretical, methodological and finally from a practical point of view. In the theoretical part, findings from the studies will be integrated in frameworks and hypotheses from the literature concerning speech perception and aging. In the methodological part, feasibility and validity of the methods used in the three studies will be considered and in the final part practical implications for the treatment and rehabilitation of presbycusis will be discussed.

3.2.1 Theoretical implications

The right auditory cortex as a locus of plasticity

A consistent finding across all three studies is that structural integrity in auditory areas in the right hemisphere is important for speech processing in older adults. While the right hemisphere has long been overlooked as a contributor to speech processing, its role in speech processing in older adulthood might be essential. In models of speech perception the main function attributed to the right hemisphere has mostly been prosody processing (Friederici & Alter, 2004; Poeppel, 2001, 2003; Ross, 1981). However, evidence from lesion-based research suggests that areas in the right hemisphere can compensate for loss of function in ipsilateral regions due to insults (Hartwigsen & Saur, 2017; Heiss & Thiel, 2006; Karbe et al., 1998; Schlaug, 2018; Thulborn et al., 1999). In the results reported in this thesis, structural integrity in areas in the right hemisphere were related to pitch discrimination (Giroud et al., n.d.), SiN perception (Keller, Giroud, & Meyer, n.d.) and dedifferentiation (Keller, Neuschwander, & Meyer, n.d.).

There are two potential interpretations to this. First, assuming that there is a general functional decline of the left hemisphere, the right hemisphere allocates resources to compensate for these losses of the left hemisphere. In that sense, individuals who are better able to initiate plastic changes in the right hemisphere are better able to compensate for declines in the left hemisphere. This plasticity could be reflected by a thicker cortex in right hemispheric auditory regions due to an increase in number of connections or increased myelination (Eickhoff et al., 2005; Rakic, 1988).

A second interpretation would be that it is not the neural processing that changes per se, but how older individuals use speech information. Based on the observation that older individuals rely more on slowly changing speech information (i.e. suprasegmental or prosodic cues, Wingfield et al., 2000) than on rapidly changing speech information, the importance of right hemispheric areas for speech processing in older adults could reflect an increased importance of TE in older adulthood. In other words, if slowly changing speech information is more important then areas related to the processing of

such information, that is auditory regions in the right hemisphere (Friederici & Alter, 2004; Poeppel, 2001, 2003; Ross, 1981) become more important too. In this case, the increased right lateralization would not reflect a compensation of decreased neural processing, but a reflection of speech perception strategies in older adults.

These two interpretations are, however, not necessarily mutually exclusive. For example, it is conceivable that neural processing deficits for rapidly changing speech information (Anderson et al., 2012) lead to changes in the use of temporal speech information which in turn leads to a stronger involvement of right hemispheric areas in spoken language processing.

Extending models of neural speech processing and funtional brain aging

The results obtained in this thesis have implications for functional neuroanatomical models of speech perception in older adulthood. On the level of initial spectrotemporal auditory processing the results from this thesis strongly suggest that existing models need to be refined and extended to account for the observations made in older adults. In particular in *Study III* the results obtained in younger adults (Liem et al., 2014) could not be replicated. Specifically, rightward lateralization in the processing of suprasegmental speech information was not evident in older adults. In general, this reflects findings from other domains (cfg. Cabeza, 2002; Reuter-Lorenz & Park, 2014) and from speech perception (Bellis et al., 2000; Goossens et al., 2016) where reduced asymmetries have been reported. One interpretation of these kind of lateralization patterns is that they reflect a compensation effort (Cabeza, 2002). According to this hypothesis, additional neural resources are recruited from homologous areas in the contralateral hemisphere.

However, the observation from *Study III* contradicts this assumption. There was evidence against a benefit in performance with reduced lateralization. Rather it seemed that the lateralization pattern was related to dedifferentiation. Participants who showed a more stable pattern of lateralization performed better in the tasks. Thus, assumptions about asymmetries from models such as the AST framework are not directly applicable to older adults. However, it should be noted that this does not necessarily apply to other aspects of the model such as relation between neural oscillations and temporal speech information, since this was not tested.

The role of the prefrontal cortex

There have been inconsistencies in previous studies about the role of the frontal cortex in speech perception in older adulthood (Giroud, Hirsiger, et al., 2018; P. C. Wong et al., 2010). According to one hypothesis, activity in the prefrontal cortex in older adults reflects a compensation strategy when sensory regions decline (Cabeza et al., 1997; Grady et al., 1994). However, frontal regions show the highest rate of atrophy (e.g. Fjell

et al., 2009) and it thus seems unlikely that compensation takes place in these regions. In addition, in some cases frontal regions were not related to auditory performance (Giroud, Hirsiger, et al., 2018). Results from this thesis offer a potential explanation for these inconsistencies. It seems that frontal regions are important for adults who suffer from sensory decline but the relation between structural integrity of these regions and speech performance is strongest for individuals with good cognitive abilities, in particular WM.

This suggests a more complex interplay between frontal compensation and speech perception including sensory decline and cognitive abilities and speaks against the notion of the prefrontal cortex as a universal compensation hub as implied by some models, such as HAROLD and PASA. In other words, frontal compensation might only come into play under certain circumstances, i.e. when there is a loss in sensory functions but still good WM capacity.

CT as a marker for structural plasticity

Another consistent finding across the three studies and in earlier work (Bermudez et al., 2008; Giroud, Hirsiger, et al., 2018) is that the anatomical measure most relevant for behaviour in older adults seems to be CT. While CSA seems to be relatively unaffected by environmental influences and lifespan experiences, plastic processes seem to be reflected by CT. In general, cortical atrophy is evident in older populations in terms of thinner cortices, as evident by the results obtained in the studies reported in this thesis. In contrast, only few age-related differences were found for CSA.

This further strengthens the argument that CT and CSA should be considered to represent different anatomical properties (Meyer et al., 2014). In addition, CT predicted several behavioural and functional variables related to speech perception within older individuals. This underlines the importance of structural plasticity for speech perception in older adulthood.

Towards an integrated view of presbycusis

Overall, one major implication of this thesis is that the results obtained therein support the framework put forward by Humes et al. (2012). Central, cognitive and peripheral factors have been found to be related to speech perception in older adulthood. Thus, in order to understand speech perception difficulties in older adulthood it is important not only to focus on peripheral measures but also considering central factors and cognition, where central factors could be either functional measures, such as neurophysiological or hemodynamic responses or measures of brain anatomy.

3.2.2 Methodological implications

Integrating structure, function and behaviour

The results from the studies of this thesis included observations of brain structure and function and behaviour. *Study I* demonstrated that brain anatomy is related to behaviour and electrophysiological brain function, *Study II* demonstrated that brain anatomy is related to behaviour and *Study III* demonstrated a relationship between hemodynamic brain activation and speech perception and between brain activation and brain structure.

Thus, the interplay between brain structure and function seem to give rise to behaviour. Especially for populations susceptible to atrophy, such as older individuals, the consideration of brain structure is relevant. On the other hand behavioural results can inform about the significance of observation from function and structure. For instance, in *Study III*, the relationship between behaviour and function suggested that the observed pattern was presumably due to dedifferentiation and did not reflect a compensation mechanism. Hence, behaviour, brain structure and function should ideally be considered altogether in work investigating speech perception.

In this context, the results obtained in the empirical work presented here support the hypothesis that different measures of brain anatomy provide different information. In particular, thickness and surface of the cortex seem to reflect independent traits and to have different relationships for speech perception. Thus, it seems to be advisable, given the results here, to refrain from investigating measures that do not consider this independence, such as measures of volume. Instead, especially given the importance of CT for aging and plasticity it seems reasonable to adopt approaches that consider these independent anatomical traits.

The significance of replication studies

Two of the three studies of this thesis were conceptual replications of previous studies. *Study II* was an attempt to replicate the results reported by Giroud, Hirsiger, et al. (2018) and P. C. Wong et al. (2010) with slightly different methods. *Study III* was an attempt to replicate the results reported by Liem et al. (2014) in a different population. Both of these studies provided valuable insight. In *Study II* potential explanations for diverging results reported by Giroud, Hirsiger, et al. (2018) and P. C. Wong et al. (2010) were suggested. In *Study III* this provided evidence that unlike in younger adults, processing in older adults is not lateralized.

Replications are an integral part of the scientific method and are vital to evaluate the reliability and robustness of an assumed effect. This is particularly meaningful given that the field of Psychology is experiencing a confidence or replication crisis, including neuroscientific studies (Button et al., 2013). While in the face of this crisis the need for replication studies is apparent only few replication studies exist within the field of

neuroscience (Evans, 2017) and few journals explicitly state that they welcome replication studies (Yeung, 2017). However, the potential of replication studies to produce new knowledge and hypotheses should not be neglected.

Overcoming the file-drawer problem

Apart from being a conceptual replication, *Study III* used a Bayesian statistical approach. Using Bayesian approaches has desirable advantages over the traditional null-hypothesis significance testing (NHST). The NHST framework is poorly suited to falsifying the alternative hypothesis and confirming the null-hypothesis (Konijn, van de Schoot, Winter, & Ferguson, 2015). In the case of a failure to reject the null-hypothesis, NHST leaves the researcher with the same amount of knowledge they had before conducting the study. In other words, it is not known whether one failed to reject the null-hypothesis because the effect that was looked for does not exist or to an inability to detect the effect, that is because of a lack of statistical power (Dienes, 2014).

This circumstance is a main reason for the emergence of the file-drawer problem (Rosenthal, 1979), which describes the situation of a bias in published results in favour of significant results (i.e., the rejection of the null hypothesis) in academia. This results in the assumption of existence of an effect even when it is not real (i.e. at a significance level of .05 and in the situation where there is no real effect, still 5% of all studies investigating this effect would find a significant result and would then presumably be published) or the overestimation of effect sizes (i.e. significant effects in underpowered studies are often due to an overestimation of the effect size).

With Bayesian hypothesis testing, these issues can be circumvented since it offers a statistical framework to obtain evidence in favour of the alternative and the null hypothesis. Within this framework, relative evidence for the null and the alternative hypothesis is obtained. In other words, it is possible to make statements about which hypothesis is more likely and to quantify this likelihood. This numerical quantity is called Bayes factor (BF).

Apart from being able to quantify evidence in favour of the null, Bayesian hypothesis testing is less susceptible to false positive results, since in contrast to p-values the BF is less susceptible to statistical power (Dienes, 2014). This seems to be especially relevant for neuroscience because a lot of neuroscientific studies are severely underpowered (Button et al., 2013).

Towards a better methodology

The work included in this thesis represents several crucial methodological features. Brain structure, brain function and behaviour are tightly intertwined and considering these factors independently is not considered a fruitful approach. Further, replication studies

and statistical analysis that can alleviate the crisis Psychology finds itself in at the present time are direly needed. Studies reported here are among the first to adopt such approaches in the field of neuroscience and thus represent an innovative strategy.

3.2.3 Practical implications

Diagnostic of presbycusis

This thesis provided supporting evidence in favour of the notion that hearing difficulties in older adults cannot be explained entirely by peripheral presbycusis (Giroud, Hirsiger, et al., 2018; Humes et al., 2012). These results seriously challenge the practice of assessing presbycusis by means of pure-tone audiometry. While capturing some facets of presbycusis, this procedure is clearly not sufficient to describe the pathology in its entirety. Thus, the results presented here add to previous research (e.g. Giroud, Hirsiger, et al., 2018), indicating the need for additional measures to get a clearer picture of an individual's hearing status.

A first step might be to include supra-thresholds measures (e.g. Lecluyse & Meddis, 2009; Lecluyse et al., 2013) into the diagnostic of hearing problems in older adulthood. In addition, measures of brain function and structure might be considered as diagnostic tools in the context of presbycusis. While this might not be feasible at the time, advances in increasing the mobility of devices measuring brain function or structure, for example mobile EEG, might be valuable assets in a clinical setting in the future. Further, accumulated research of the field indicates that the symptom complex of presbycusis is heterogeneous and that a shift towards a more individualized diagnostic is desirable.

Treatment of presbycusis

As a result of the predominant use of pure-tone audiometry in diagnostics and the lack of alternative procedures, the dominant treatment for presbycusis is the application of hearing aids. While hearing aids can ameliorate the symptoms of presbycusis a more individualized treatment of a persons symptoms would be desirable too. One option for treatment could be auditory trainings related to temporal processing or neuromodulatory approaches to counteract functional deterioration. In general, the results of this thesis indicate the need for advances in diagnostic and treatment of presbycusis to better account for the heterogeneity of phatologies. However, at this point, reliable and valid approaches still remain to be developed.

3.3 Open questions and future directions

In this section open questions related to the empirical work presented here are identified. Several theoretical and methodological issues are discussed. Future perspectives and potential research directions are proposed.

3.3.1 Performance and strategy

One question that was left open by *Study I*, was whether the higher neural sensitivity for prosodic speech cues is directly reflected by behavioural differences. It has been stated that, differences in sensitivity to acoustic cues do not always translate into behaviour (Steinhauer et al., 2010). However, the finding that older adults are worse at discriminating pitch differences seems at odds with the notion that they are more sensitive towards those kind of cues. But can it be expected that higher sensitivity leads to better performance and is this what we want to know?

Higher neural sensitivity to prosodic cues might reflect that older adults rely more on slowly changing speech information and their neural networks are tuned to this auditory cues. In that sense, a higher preference for prosodic cues doesn't necessarily mean that these are perceived better. While it is certainly important to identify domains where older adults perform worse than younger individuals in order to identify where difficulties inherent to presbycusis lie, it might also be purposeful to ask how different age groups use speech information and how this is reflected in neural processing. So instead of asking whether different neural processing leads to better or worse performance, the question could also be whether different neural processing leads to different use of speech information (or vice versa).

Thus, it might be that the relations between neural processing and behaviour is stronger for tasks measuring preferences for speech information. In general, future studies will have to provide insights into whether differences in neural processing reflect differences in performance, or differences in preferences or speech perception strategies, respectively.

3.3.2 Disentangling sensory decline, cognition and brain structure

The results from *Study II* suggested a relationship between sensory decline, cognition, brain structure and SiN perception. However, a relationship between PTA and cognition based strategies was not obtained in a direct way.

Thus, one thing left to do is to confirm that this relationship exists, by investigating larger samples of older adults with various levels of hearing thresholds. Based on the results obtained within this thesis it would be expected that the relationship between

cognition related areas, such as the SFG, would be more pronounced in individuals with increased sensory decline. The same is true for the relation between cognitive abilities, brain anatomy and SiN perception. Further research is needed to get a clearer picture of the relationship between brain anatomy and cognitive abilities and its consequences for SiN perception. The expectation here would be that cognitive strategies are predominantly used by individuals whose abilities are still good enough to be able to counteract sensory decline.

In this thesis the ability most closely related to SiN perception was WM. However, this does not mean that other cognitive abilities are unrelated to speech comprehension and brain anatomy in older adulthood. Investigating the potential influences of various cognitive abilities is an endeavour that remains to be done.

A further point that needs to be clarified is what happens if sensory functions and cognitive abilities are low too (see Figure 3.1). It might be that individuals try to engage bottom-up as well as top-down processes or either one of the two.

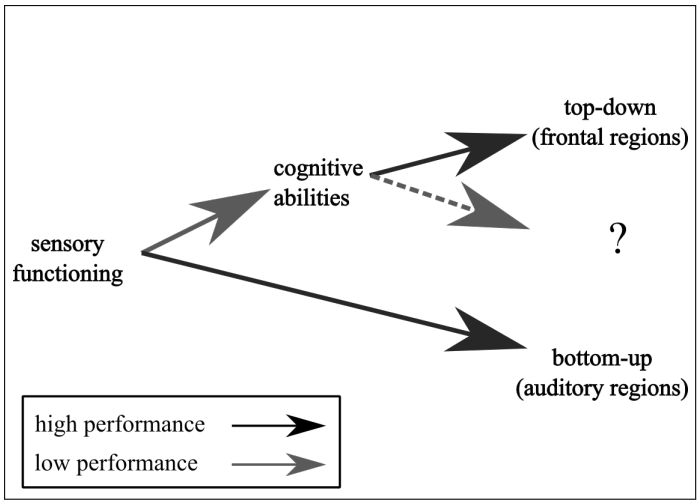

Figure 3.1. Possible relation between sensory function, cognitive abilities and speech processing. Individuals with high sensory abilities rely on bottom-up processing and auditory regions. If sensory functions are low, processing happens in a more top-down manner. It is unclear what happens if both, sensory and cognitive abilities, are low.

In general a complex pattern of interactions between cognition, presbycusis and brain anatomy in relation to SiN perception seems to emerge. Disentangling these factors will have to be the task of future work.

3.3.3 Dedifferentiation in speech perception

The results obtained in *Study III* suggest that dedifferentiation phenomena play an important role in speech processing. Not much is known so far however about this kind of age-related changes in neural processing in the domain of speech perception. It is, for example, unclear whether dedifferentiation can only be observed in elementary speech

processing, such as the spectrotemporal analysis of the speech signal, or whether this also applies to higher-level language functions, such as syntactic processing. Another question pertains to the relationship between brain structure and dedifferentiation.

Thus far, only little knowledge exist about the relationship between cortical atrophy and loss of specificity in neural responses. The evidence acquired in this thesis and by others (Voss et al., 2008), point towards increased neural dedifferentiation with higher cortical atrophy. Thus, one hypothesis would be that cortical atrophy leads to less specific neural responses and will have to be investigated more closely in the future. Another circumstance that was evident in *Study III* was that models of speech perception based on younger populations are probably ill-suited to describe spoken language processing in older adults. Future research will have to work towards building comprehensive models of neural speech processing in older adults that help in guiding diagnosis and therapy of presbycusis.

3.3.4 Longitudinal studies

All the work included in this thesis is based on cross-sectional data. In order to gain knowledge about trajectories and causal interrelationships between factors related to presbycusis it is desirable to move on from cross-sectional towards longitudinal studies.

The study of the life-span is inherently a study of change. A major aim is to describe these changes and identify factors that influence when and how these changes happens. The only way to accurately describe such changes is by observing individuals repeatedly over a certain time span. Not only will this lead to a better understanding about the changes individuals undergo along their lifespan but it will also help clarify causal relationships between factors that are difficult to experimentally manipulate. A prime example of such a relationship is the relationship between presbycusis and brain anatomy. One question is for example whether changes in hearing lead to changes in brain structure or whether changes in brain structure lead to changes in hearing. Answering questions like these requires to embrace longitudinal designs.

3.4 Concluding remarks

The diagnosis, therapy and rehabilitation of presbycusis profits from accurate models. In the case of hearing and speech understanding in older adulthood, these models were based solely on peripheral hearing for the most time. Among other work, this thesis laid out reasons and empirical evidence that strongly suggest to move beyond measures of hearing thresholds in order to come up with more comprehensive, better models of speech perception in older adulthood.

Thus, the work included in this thesis contributes to a better understanding of hearing and speech comprehension in older adulthood and will hopefully help to establish new models thereof that can guide rehabilitation and therapy and ultimately enable people to lead lives of high well-being across the entire lifespan. Given that presbycusis is among the most common conditions for individuals above the age of 65 years and that demographic changes suggest that the number of people belonging to this population will continuously grow in the years to come, the study of hearing and aging is of paramount importance.

Not being able to communicate means having to give up a big part of personal independence and missing out on social interactions. Preventing the loss of social integration is essential for people to lead a healthy, stable and fulfilling life, especially when they grow older.

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Curriculum Vitae

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COMPETITIVE INTRAMURAL FUNDING

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FELLOWSHIPS

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PUBLICATIONS

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TALKS (* presenting author)

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Keller, M*. *(May 2017). Speech processing in older adults* Invited presentation at the Team meeting of Prof. Dr. Thad Polk, Computational and Cognitive Neuroscience Lab, University of Michigan, USA

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POSTER PRESENTATIONS (* presenting author)

Keller, M*. *& Meyer, M. (2017). Hemispheric Lateralization of Speech processing in older Adults?* Poster and short talk presented at the LIFE Spring Academy 2017 Ann Arbor, Michigan, May 2017

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Keller, M*. *& Meyer, M. (2015)."The triangle of speech comprehension in older age: neuronal, cognitive, and audiometric contributions to elemantary speech processing",* Poster, LIFE Fall academy 2015 Castle of Marbach, October 2015

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Effects of age-related changes in inhibitory neurotransmitters on auditory speech processing
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